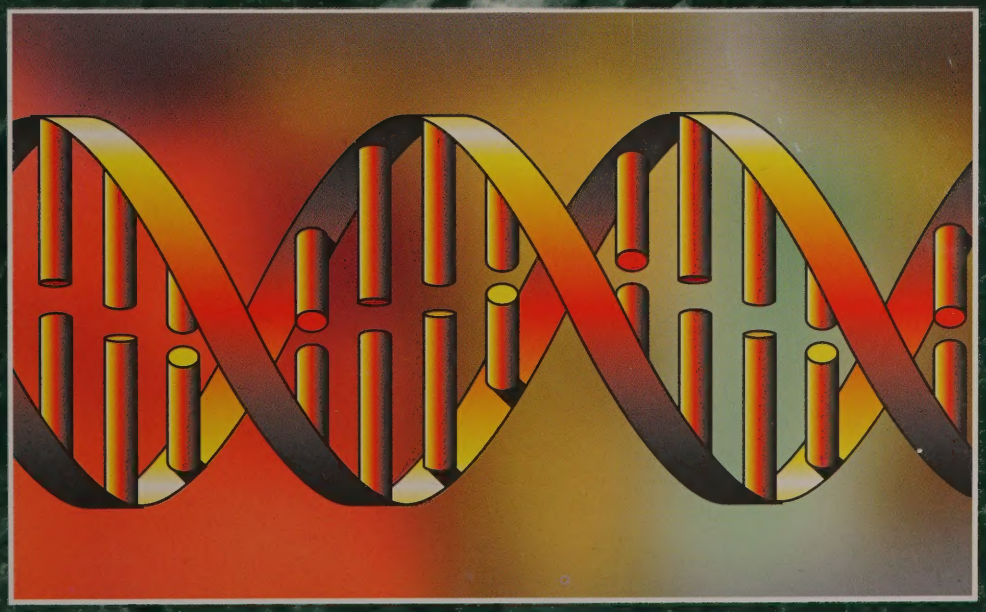
HSE
Health & Safety Executive

A guide to the Genetically Modified Organisms (Contained Use) Regulations 1992, as amended in 1996



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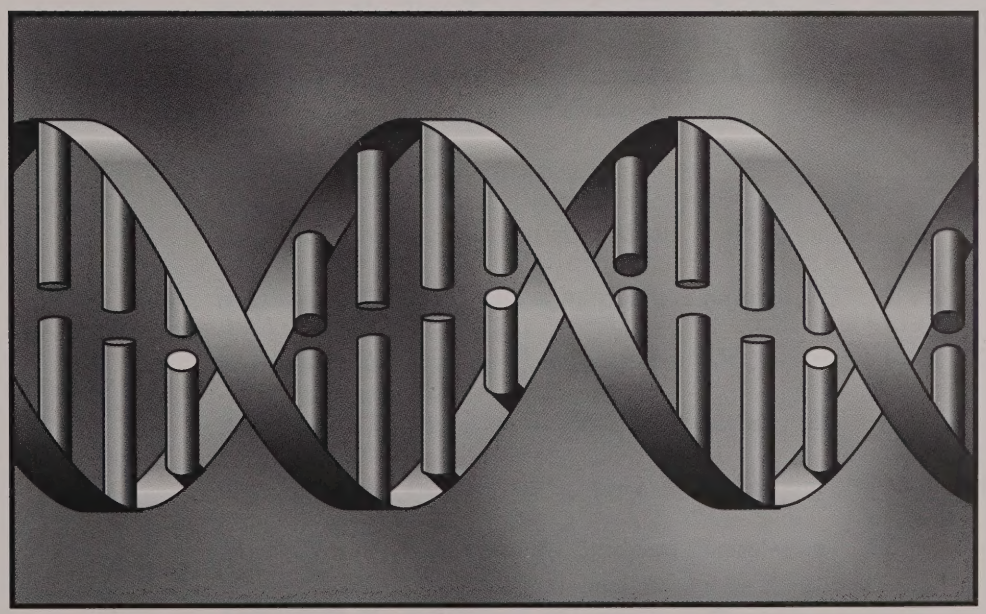

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This guide explains in non-legal language what the law requires you to do. It also includes guidance on how to comply with the law to which the following paragraph is applicable.

This guidance is issued by the Health and Safety Executive. Following the guidance is not compulsory and you are free to take other action. But if you do follow the guidance you will normally be doing enough to comply with the law. Health and safety inspectors seek to secure compliance with the law and may refer to this guidance as illustrating good practice.

Contents

Introduction

1 This booklet gives new practical guidance on the Genetically Modified Organisms (Contained Use) Regulations 1992 (SI 1992/3217) (the Contained Use Regulations) as amended by the Genetically Modified Organisms (Contained Use) (Amendment) Regulations 1996 (SI 1996/967), which are designed to ensure the safe use and handling of genetically modified organisms (GMOs) under containment. For ease of reference the Regulations quoted combine the text of the 1992 and 1996 Regulations.

2 The Contained Use Regulations implement within Great Britain Council Directive 90/219/EEC on the contained use of genetically modified micro-organisms (GMMs), which was adopted on 23 April 1990 (OJ No L117, 8.5.90, p1), as amended by Commission Directive 94/51/EC (OJ No L297, 18.11.94, p29), adopted on 7 November 1994.

3 The Regulations have been made under the powers of the Health and Safety at Work etc Act 1974 (the HSW Act) and the European Communities Act 1972 and are concerned with protecting both human health and the environment. They require, with certain exceptions, that anyone carrying out any activity involving genetic modification does so in conditions of contained use which satisfy the Regulations. Among other things this means carrying out a risk assessment, and in certain circumstances submitting a notification to the Health and Safety Executive, and in certain circumstances receiving the Executive's formal consent.

4 For GMMs the Regulations cover both human health and environmental risks. For larger genetically modified organisms, such as plants and animals, they cover human health risks only. The environmental risks associated with work with larger organisms are covered separately by section 108(1)(a) of the Environmental Protection Act 1990 (the EP Act). This section requires anyone creating a genetically modified organism which is not an approved product under the Genetically Modified Organisms (Deliberate Release) Regulations 1992 (the Deliberate Release Regulations), or obtaining one from elsewhere, to carry out an assessment of the environmental risks. The Genetically Modified Organisms (Risk Assessment) (Records and Exemptions) Regulations 1996 (SI 1996/1106), which replace the Genetically Modified Organisms (Contained Use) Regulations 1993 (SI 1993/15), require records on the risk assessment to be kept for 10 years.

Other relevant legislation

5 Note that this guidance does not cover other legislation which may also have a bearing on work with genetically modified organisms. That legislation includes, for example, controls on:

(a) human and veterinary medicines, under the Medicines Acts 1968 and 1971 and European Council Regulation No (EEC) 2309/93;

(b) pesticides, under the Food and Environment Protection Act 1985;

(c) plant pathogens and genetically modified material and plants under the Plant Health (Great Britain) Order 1993 and Plant Health (Forestry) (Great Britain) Order 1993;

(d) transgenic animals under the Animals (Scientific Procedures) Act 1986; and

(e) the introduction of non-indigenous species under the Wildlife and Countryside Act 1981.

All this legislation remains in force and is not affected by the Contained Use Regulations which deal specifically with genetic modification. In addition, all work activities, including those concerned with genetic modification, are covered by the HSW Act and relevant regulations made under that Act, including, where appropriate, the Control of Substances Hazardous to Health Regulations 1994 (SI 1994/3246) (which include provisions relating to biological agents) and the Management of Health and Safety at Work Regulations 1992 (SI 1992/2051). For genetic modification procedures which involve the use of plant pathogens or plant pests in England, please contact:

Ministry of Agriculture Fisheries and Food
Plant Health Division
Room 331
Foss House
1-2 Peasholme Green
York YO1 2PX

In Scotland the contact address is:

Scottish Office
Agriculture Environment and Fisheries Department
Pentland House
Room 356
47 Robbs Loan
Edinburgh EH14 1TW

Legislation on the deliberate release of genetically modified organisms

6 A second EC Directive, 90/220/EEC, deals with the deliberate release into the environment of genetically modified organisms. Regulations to implement this Directive - the Genetically Modified Organisms (Deliberate Release) Regulations 1992, as amended by the Genetically Modified Organisms (Deliberate Release) Regulations 1995 - have been introduced under the EP Act. Separate guidance on the Act and Regulations has been produced by the Department of the Environment. DoE/ACRE Guidance Note 2 deals with the EP Act and the 1992 Regulations, and DoE/ACRE Guidance Note 7 with the 1995 Regulations. Further details can be obtained from the DoE Biotechnology Unit, Room B353, Romney House, 43 Marsham Street, London SW1P 3PY (Tel: 0171 276 8187, Fax: 0171 276 8333).

Enquiries on the Contained Use Regulations

7 For further advice on any aspects of the Contained Use Regulations or the guidance in this booklet, please contact the Health and Safety Executive at either of the following addresses:

Health Directorate Division B
Rose Court
2 Southwark Bridge
London SE1 9HS
Tel: 0171 717 6297/6348
Fax: 0171 717 6199

Division of Science and Technology, E4
Magdalen House
Stanley Precinct
Bootle
Merseyside L20 3QZ
Tel: 0151 951 4831
Fax: 0151 951 3474

Summary

8 The main requirements of the Contained Use Regulations provide for:

(a) human health and environmental risk assessment;

(b) records of risk assessments;

(c) establishment of a local genetic modification safety committee to advise on risk assessments;

(d) categorisation of work on the basis of risks to human health and safety and of risk of damage to the environment, taking into account the nature of the organism and the type of activity;

(e) advance notification to the Health and Safety Executive (HSE) of an intention to use premises for activities involving genetic modification for the first time and, for some activities, consent from HSE before work can start;

(f) notification to HSE of individual activities involving genetic modification, and, for some activities, consent from HSE before they can proceed;

(g) standards of occupational and environmental safety and levels of containment;

(h) notification of accidents and, where appropriate, the drawing up of emergency plans;

(i) disclosure of information and public registers, with provision for confidentiality;

(j) fees for notifications.

9 The activities covered by the Contained Use Regulations include laboratory operations, housing and/or breeding of modified animals in animal houses or farm animals restrained by fencing (provided they are not shedding genetically modified micro-organisms without sufficient biological or chemical barriers), the use of growth rooms and glasshouses of appropriate specification, and the use of fermenters. All such activities are prohibited unless they are carried out in conditions of containment which comply with the Regulations.

10 'Contained use' is defined as any operation in which organisms are genetically modified or in which GMOs are cultured, stored, used, transported, destroyed or disposed of and for which physical barriers, or physical barriers combined with chemical or biological barriers or both, are used to limit their contact with the general population and the environment. Note that physical barriers appropriate to the GMO must always be present. In some cases physical barriers alone may not limit contact with the environment sufficiently; for example, some designs of glasshouse may not adequately contain plant pollen.

11 The Contained Use Regulations cover the breeding on of a genetically modified plant or animal, as well as activities involving modified organisms supplied by others. They do not cover the deliberate release of GMOs to the environment for experimental purposes or the marketing of products for deliberate release consisting of, or containing, GMOs. These activities are covered by the EP Act and the Deliberate Release Regulations.

12 So long as a product and its use are as specified by a consent under the Deliberate Release Regulations or relevant product legislation in the conditions

for marketing, it will not be covered by the Contained Use Regulations. Breeding on from such 'approved products' may be allowed under the conditions for marketing and in such cases would not be further regulated under the Deliberate Release Regulations or the Contained Use Regulations.

Administrative arrangements

13 The Contained Use Regulations are administered jointly by HSE and the Department of the Environment (DoE), but duty-holders have a single point of contact in HSE. All notifications under the Contained Use Regulations should be made to HSE, which has a duty to pass copies to the Secretary of State for the Environment (or the Secretary of State for Scotland or Wales as appropriate). The agreement of the Secretary of State must be obtained before HSE can issue a consent, insofar as it relates to environmental protection. Interdepartmental arrangements have been set up to ensure that on environmental matters HSE will co-operate with the Secretary of State in putting the Regulations into effect. Where the Secretary of State requires further information about environmental aspects of notifications involving the use of genetically modified micro-organisms, or where HSE requires further information about human health aspects of any notification, it will be requested by HSE.

14 Notifications and consent applications must be made in a form approved by the Health and Safety Executive. Applications should be submitted to:

Directorate of Science and Technology, E4
Magdalen House
Stanley Precinct
Bootle
Merseyside L20 3QZ
Tel: 0151 951 4831
Fax: 0151 922 7918

Approved forms for notifications can be obtained free from the above address.

Enforcement

15 Enforcement of the Contained Use Regulations is the responsibility of HSE. HSE inspectors have extensive powers under the HSW Act, including powers to enter premises and to require the provision of information relevant to their purposes and the production of documents.

Guidance from the Advisory Committee on Genetic Modification

16 HSE, with advice from the Advisory Committee on Genetic Modification (ACGM), has prepared guidance on subjects related to the contained use of GMOs. It is referred to, where appropriate, in the guidance that follows and a list of current subjects covered is in Appendix 2. The guidance is updated from time to time and copies may be obtained from HSE's Division of Science and Technology, E4 (address in paragraph 14) or HSE's Health Directorate (see address in paragraph 7).

Regulation 1

Citation and commencement

Regulation 1

These Regulations may be cited as the Genetically Modified Organisms (Contained Use) Regulations 1992 and shall come into force on 1st February 1993.

Guide 1

17 These Regulations have now been amended by the Genetically Modified Organisms (Contained Use) (Amendment) Regulations 1996 which came into force on 27 April 1996.

Regulation 2

Interpretation

Regulation

(1) In these Regulations, unless the context otherwise requires -

"the 1989 Regulations" means the Genetic Manipulation Regulations 1989[(a)];

"accident" means any incident involving a significant and unintended release of genetically modified organisms in the course of an activity involving genetic modification which presents an immediate or delayed hazard to human health or to the environment;

"approved" means approved in writing for the time being by the Executive;

"activity involving genetic modification" means any operation involving the contained use of a genetically modified organism;

"the Agreement" means the Agreement on the European Economic Area signed at Oporto on 2nd May 1992, as adjusted by the Protocol signed at Brussels on 17th March 1993 and adopted as respects the United Kingdom by the European Economic Area Act 1993[(b)];

"contained use" means any operation in which organisms are genetically modified or in which such genetically modified organisms are cultured, stored, used, transported, destroyed or disposed of and for which physical barriers or a combination of physical barriers with chemical or biological barriers or both, are used to limit their contact with the general population and the environment;

"the contained use Directive" means Council Directive No 90/219/EEC[(c)] on the contained use of genetically modified micro-organisms;

"the European Economic Area" means the Area referred to in the Agreement;

"the Executive" means the Health and Safety Executive;

"genetic modification" in relation to an organism means the altering of the genetic material in that organism by a way that does not occur naturally by mating or natural recombination or both and within the terms of this definition -

(a) genetic modification occurs at least through the use of the techniques listed in Part I of Schedule 1; and

(b) the techniques listed in Part II of that Schedule are not considered to result in genetic modification,

(a) SI 1989/1810.
(b) 1993 c.51.
(c) OJ No. L 117, 8.5.90,p.1.

2

Regulation

and "genetically modified" shall be construed accordingly;

"genetic modification safety committee" means the committee established in accordance with regulation 11;

"member State" means a State which is a Contracting Party to the Agreement;

"micro-organism" means a microbiological entity, cellular or non-cellular, capable of replication or of transferring genetic material including animal or plant cell cultures;

"organism" means a biological entity capable of replication or transferring genetic material and includes a micro-organism, but does not include a human or a human embryo;

"self-cloning" means the removal of nucleic acid from a cell or organism, followed by the re-insertion of all or part of that nucleic acid - with or without further enzymic, chemical or mechanical steps - into the same cell type (or cell-line) or into a phylogenetically closely related species which can naturally exchange genetic material with the donor species;

"Type A operation" means any activity involving genetically modified micro-organisms for the purposes of teaching, research, development, or for non-industrial or non-commercial purposes on a scale at which the practices and conditions of the operations relative to the culture volume and numbers of organisms involved is such that -

(a) the system used to keep the organisms under containment reflects good microbiological practice and good occupational safety and hygiene; and

(b) it is possible easily to render the organisms inactive by standard laboratory decontamination techniques;

"Type B operation" means any activity involving the genetic modification of micro-organisms other than a Type A operation.

(2) Genetically modified organisms shall be classified -

(a) in the case of micro-organisms -

(i) as Group I micro-organisms if they satisfy all of the criteria set out in Part I of Schedule 2, or

(ii) as Group II micro-organisms if they do not satisfy all of the said criteria; or

(b) in the case of genetically modified organisms other than micro-organisms, as satisfying the criteria set out in Part II of Schedule 2 if they so satisfy those criteria.

(3) In these Regulations, unless the context otherwise requires -

(a) a reference to a numbered Part, regulation or Schedule is a reference to the Part, regulation or Schedule in these Regulations so numbered; and

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(b) a reference to a numbered paragraph is a reference to the paragraph so numbered in the regulation or Schedule in which that reference occurs.

18 **'Contained use'** covers any operation involving GMOs under the conditions of containment laid down by the Regulations. The containment must be provided by physical barriers, whether or not they are supplemented by chemical or biological ones; the containment must limit the contact of the genetically modified organism with the general population and the environment.

19 The definition of **'genetic modification'** includes any alteration of the genetic material (DNA or RNA, also referred to as 'heritable material') of an organism by a way that could not occur naturally by mating and/or recombination. Note that it is not the techniques which are controlled but activities involving the GMOs or GMMs which are created by using the techniques. Some examples of techniques included in the definition are listed in Schedule 1 Part I, however:

(a) the list is not exhaustive;

(b) gene deletions or the insertion of multiple copies of a gene count as genetic modification if they are brought about using any listed technique (see also paragraph 24);

(c) techniques involving the direct introduction of heritable material include such things as particle bombardment of plant tissues, direct injection of naked DNA into an animal and the use of other gene delivery systems such as liposomes (but see the definition of 'organism' in paragraph 23 which clarifies the position of human gene therapy using these techniques);

(d) cell fusion is a technique of genetic modification if it is achieved in a way that does not occur naturally. There are some exceptions to this (see regulation 3).

20 Schedule 1 Part II lists techniques which are not considered to fall within the definition of genetic modification if they do not involve the use of recombinant DNA molecules or genetically modified organisms. So, for example, the transformation of bacterial cells with DNA or the transformation of cells with viruses (transfection) do not count as genetic modification unless modified DNA or modified viruses are employed or the recipient is itself genetically modified.

21 Schedule 1 Part III lists techniques which are considered to be genetic modification but which are excluded if they do not involve the use of genetically modified organisms as recipient or parental organisms (see guidance on regulation 3).

22 **'Micro-organism'** covers all micro-organisms. The term includes viruses and viroids, the uncharacterised agent responsible for transmissible spongiform encephalopathy, cell cultures and tissue cultures, including those from plants, animals and humans. It does not cover, for example, naked nucleic acid, plasmids or liposome gene delivery systems.

23 **'Organism'** covers, in addition to all micro-organisms, all multicellular organisms not defined as micro-organisms, including plants and animals but not including humans or human embryos.

24 **'Self-cloning'** is one of the techniques referred to in Schedule 1 Part III. This term covers the reinsertion of an organism's nucleic acid into the same species or into a phylogenetically closely related species with which it can naturally exchange genetic material. The nucleic acid may have been subject to

modification by enzymic, chemical or mechanical steps so as to produce a novel order of genes/bases, to remove sequences, to produce multiple gene copies etc. Self-cloning of micro-organisms where the resulting organism is unlikely to cause disease (for further guidance see the section on the Group I classification, in paragraphs 28 to 53) or of organisms which meet the criteria in Part II of Schedule 2 is exempt from the Regulations.

25 **'Type A operation', 'Type B operation'**. All activities involving genetically modified micro-organisms have to be classified as either Type A or Type B. This classification does not apply to genetically modified animals and plants (non-micro-organisms). Criteria for Type A operations are defined: all activities which are not Type A are automatically Type B. In order to be classified as Type A an operation must fulfil two tests: one of **purpose** and one of **scale**. Both tests must be passed for Type A classification:

(a) **test of purpose**. The simplest way to approach the test of purpose is to decide if the activity being undertaken is for any one (or more) of the following:

(i) teaching;
(ii) research;
(iii) development;
(iv) non-industrial;
(v) non-commercial.

If any of these apply, the activity may, subject to the test of scale below, be classified as Type A. Only if the activity is for none of the above does it fail the test of purpose and thus is automatically Type B;

(b) **test of scale**. This determines whether or not the activity is 'small-scale'. What counts as 'small' is not set by a fixed culture volume but depends on the systems of control. Type A operations must be of a scale where the appropriate work practices are such that:

(i) the system used to keep the organisms under containment reflects good microbiological practice and good occupational safety and hygiene; and

(ii) it is possible easily to render the organisms inactive by standard laboratory decontamination techniques.

It will be particularly important to consider whether, in the event of complete failure of the primary containment, the secondary containment is sufficient to contain the culture and also to allow for it to be **easily** inactivated by standard laboratory techniques.

26 **Type A** operations typically involve small numbers of organisms. The work can be basic science or applied research, in a laboratory in either an academic institution or a commercial firm and may include development of a process for subsequent industrial or commercial exploitation.

27 A **Type B** operation is any operation which does not fulfil the criteria for Type A. Type B operations will in the main be carried out under industrial conditions. Usually the production volume is considerably greater than in Type A operations and operational conditions are different, but all operations which produce an industrial and commercial product are Type B operations even though they may be carried out at small volume. A Type B operation which is industrial production is likely to be a process or series of processes repeated again and again with little or no change in process conditions, and

leading to a product that is either put on the market or used as a raw material elsewhere in the production process. Certain large-scale research activities will also be Type B.

Classification of genetically modified micro-organisms

28 The Regulations define two groups of GMMs, **Group I** and **Group II** . All persons undertaking contained use must classify the GMM into one of these groups.

29 Schedule 2 sets out the criteria that a GMM must meet to be classified as Group I. Those that do not meet these criteria are Group II. Guidelines for the further interpretation of these criteria are published in a European Commission Decision No. 96/134/EC which is reproduced in Appendix 1. The guidance and examples set out below are intended to incorporate, explain further and expand the criteria and guidelines.

Guidance

Criteria for the classification of GMMs

30 The classification is made by considering the recipient or parental (host) organism, the nature, activity and function of the vector and insert sequences and the overall combination of host, vector and insert (the final GMM). **All three criteria must be met for a Group I classification.** For some GMMs a decision regarding classification will pose little difficulty; however, others will require more in-depth consideration in order to decide their Group status.

Criterion i: The recipient or parental micro-organism is unlikely to cause disease to humans, animals or plants

31 This criterion is concerned with the properties of the host (recipient or parental) organism. Some commonly-used organisms will fulfil this criterion, examples being *Saccharomyces*, *Bacillus subtilis* and eukaryotic cell lines such as Chinese Hamster Ovary (CHO) cells.

32 In determining whether a consequence might be disease (see Box 1) users should consider only those deleterious effects that might occur in healthy, immunocompetent people, animals or plants.

Example

For example, many species of bacteria and fungi are not normally considered to be pathogenic but there may be occasional reports of isolates from a gravely ill person or an unhealthy plant; this would not mean that they are 'likely to cause disease' in the general case. Further experimentation or evidence may be needed in some cases.

Box 1 The interpretation of 'disease'

Disease should be taken as meaning any disturbance of structure or function in a human, animal or plant of such a degree as to produce detectable illness or disorder. In considering whether or not disease may be caused it is important to include effects beyond infection. These might be toxic, mutagenic, tumorigenic, allergenic and other adverse biological effects that could result, for example, from the over-expression of biologically active molecules such as hormones or cytokines.

33 In many cases the capacity to cause disease can be gathered from various pathogen classification schemes. These schemes are not exhaustive. Those for animal and plant pathogens in particular tend to cover only domesticated/commercially important species. It is therefore important not to rely on these lists as the sole criteria for whether or not an organism may cause disease. As a general guide, however, the following recipient or parental organisms can be considered likely to cause disease and therefore are not compatible with this criterion:

(a) biological agents listed in hazard groups 2, 3 or 4 of the Approved List;*

(b) quarantine organisms listed in the Plant Health (Great Britain) Order 1993 or other plant pathogens or pests with susceptible UK species;

(c) organisms listed in The Plant Health (Forestry)(Great Britain) Order 1993;

(d) pathogens of animals, poultry, fish or bees controlled by the Agriculture Departments.

34 For hosts for which indicators of this sort are not available, the **likelihood** of causing disease should be estimated with no allowance being made for the provision of special containment measures or work procedures. Equally it should not be assumed that there has been unusual or gross exposure. For an organism to be considered as unlikely to cause disease it should not be capable of causing harm to a healthy person, plant or animal under any normal conditions. Examples include the result of a reasonably foreseeable incident, such as a needlestick injury, accidental ingestion, aerosol exposure, and escape leading to environmental exposure. (See also Box 2.)

Example

For example, it is not valid to say that vaccinia virus is **unlikely** to cause disease on the grounds that it will always be handled at containment level 2. Equally it cannot be assumed that *Lactobacillus* is **likely** to cause disease on the basis that if large numbers were to be injected into a new-born mouse it might cause illness or death.

Non-virulent strains of acknowledged pathogens

35 Recognising that such classification schemes are relatively imprecise and incomplete, the European Commission guidelines do allow for non-virulent strains of acknowledged pathogenic species to be considered unlikely to cause disease if one or more of the following is true:

(a) the strain has an established record of safety in the laboratory and/or industry with no adverse effects on human, animal or plant health;

(b) the strain is stably deficient in genetic material that determines virulence, or has stable mutations known to reduce virulence sufficiently.

36 Commonly used examples include: *E. coli* K-12 and its derivatives; *Agrobacterium tumefaciens* strains which carry modified plasmids deficient in all tumorigenic genes; some *Salmonella typhimurium* strains of the BRD series which contain deletions in genes for aromatic amino acid synthesis and the heat shock response such that they no longer cause disease and certain attenuated vaccine strains. Caution should be exercised with attenuated strains which are still considered to be pathogenic, for example vaccinia virus.

* Published in the *Categorisation of biological agents according to hazard and categories of containment*, 4th edition 1995, HSE Books, ISBN 0 7176 1038 1.

37 In cases in which it is not essential to remove all virulence determinants from an attenuated pathogen, particular attention should be paid to any toxin genes (whether expressed or silent), plasmid or phageborne virulence determinants and harmful adventitious agents that remain. On such occasions a case-by-case evaluation will be needed to ensure that the organism is unlikely to cause disease. Also the possibility of reversion or complementation of disabling mutations should be considered.

Box 2 The environment likely to be exposed

The European Commission guidelines indicate that in assessing the likelihood of disease or adverse effects on the environment it is necessary to consider all the organisms in the air, soil and water in the environment likely to be exposed to the GMM. For a contained use facility this will be the local area and any wider area which could reasonably be expected to be affected. If a Group I classification relies on this consideration it will be necessary to obtain information on the geographical distribution of susceptible species, and all possible modes of transmission including local drains and watercourses. However, another approach that is permissible is simply to assume that the environment likely to be exposed is the whole of the UK and to base the classification on the reasonably foreseeable effects of such a wider spread.

For example, an organism might be a specific pathogen of banana plants or olive trees, but it would not be likely to cause disease since there are few susceptible hosts in the UK.

A central consideration is the survivability of the GMM in the environment. Harm to the environment will normally only arise if a GMM can survive and possesses other hazardous characteristics. Many organisms commonly used in genetic modification cannot survive for any significant periods, and therefore the likelihood of interaction with the environment is low. Limitations to survivability might include such factors as auxotrophic mutants, sensitivity to UV, and specific growth and culture requirements.

As an extreme example, a derivative of *Clostridium tetani* defective in aromatic amino acid synthesis genes but which still expressed the tetanus toxin would clearly not be compatible with the Group I classification.

Criterion ii: The nature of the vector and the insert is such that they do not endow the genetically modified micro-organism with a phenotype likely to cause disease to humans, animals or plants, or to cause adverse effects in the environment

38 This criterion considers whether what has been modified in the organism will result in a harmful phenotype and assumes that the recombinant DNA construct consists of gene(s) that are expressed on autonomous vectors. In cases where the modification involves gene(s) being deleted or integrated into the chromosome, the discussion and examples below may not apply in full. For Criteria (ii) and (iii) 'harm' means both disease and adverse effects in the environment (Box 3). Where activities are of Type B, users should also refer to the additional considerations set out in paragraphs 51 to 54.

Box 3 Adverse effects on the environment

Criteria (ii) and (iii) also require that the organism is 'unlikely to cause adverse effects on the environment'. A degree of judgement will be needed in determining whether this is so. Further discussion of environmental harm can be found in HSE/ACGM guidance on risk assessment. Adverse effects include direct effects on organisms in the environment or interference with ecosystems and/or indirect effects which may occur at a distance from the GMM, or as a result of descendants of the GMM. In most cases effects will be considered to be adverse if they involve populations or sub-populations of organisms. However, in the case of rare or endangered species, significant harm may result if only a small number of individual organisms are affected. Examples of indirect effects are harmful alterations in the physico-chemical properties of the soil or water components of the environment or community changes because of competition effects.

When assessing whether a particular effect is likely, an important factor will be the nature of the chain of cause and effect leading to harm. A very remote effect, that is, one that depends on a long chain of causal steps, will naturally be less likely to occur (except in the rare event that every step takes place with 100% probability). An effect that depends on adventitious or rare events may also be considered unlikely. Conversely, short causal chains and inexorable connections will favour the conclusion that the envisaged effect is likely.

For example, one concern surrounding the cloning of the ice nucleation into a disabled bacterium might be that if the GMM escaped and survived in the local environment it might alter frost formation. In turn this might change the local and regional climate patterns with potentially serious long-term effects. However, because of the long causal chain with very low probability steps it is virtually impossible that it would occur. On the other hand a modified bacterium that sequestered inorganic iron very efficiently and was designed to grow in the rhizosphere of plants might be said to be likely to cause harm to the environment if it was so efficient that plant growth could be adversely affected.

39 The principal consideration is the **phenotype** of the final GMM which is endowed by the expressed vector or insert genes. Expression should be considered to include RNA transcripts (commonly used in anti-sense technology) as well as proteins and polypeptides.

40 The simplest case will be when the gene(s) are not expressed in the GMM at significant levels. This may occur because there is no active promoter, or because the inserted DNA contains introns which cannot be processed in the host organism. In such cases it can generally be assumed that the likelihood of a harmful phenotype is negligible (see also paragraphs 45 and 46 on gene transfer). In cases where no expression occurs, even a potentially harmful gene such as an oncogenic or tumorigenic sequence in a disabled bacterial host would be unlikely to endow the GMM with a phenotype likely to cause disease or to cause adverse effects on the environment.

41 If the inserted gene is expressed in the GMM, various factors will need to be considered in order to determine if the phenotype is likely to be harmful. The most obvious way in which a harmful phenotype can arise is as a consequence of the gene product having a biological activity which can act directly to cause harm to either humans or the environment. Further

information on this issue, as it applies to bacteria and cell lines, can be found in HSE/ACGM guidance on risk assessment, under the sections on Expression and Damage. However, it is also possible that a harmful phenotype can arise if the gene product can act alongside existing characteristics of the host organism and endow the GMM with altered pathogenic properties. Examples of this would be an alteration of the host range of the GMM or if the inserted DNA encoded a pathogenicity determinant capable of substituting for a disabling mutation present in the parental organism.

42 The types of gene products possessing biological activities which could act directly to cause harm include toxins, modified prion proteins and growth modulator proteins (hormones, cytokines). Proviral sequences coding for complete viral DNA should also be considered if there is any possibility of the production of infectious particles (see also paragraph 45 for further consideration). Any evaluation of the likelihood of causing disease or any other adverse consequences must consider the activity of the product, how much is produced and whether it is correctly processed or secreted by the GMM.

43 The phenotype resulting from a vector may be dependent on the recipient or parental organism. What is true for one host should not be automatically assumed when the construct is transferred to a different host.

Example

For example, a disabled retrovirus vector in bacteria or most cell lines would be incapable of producing infectious virus particles. However, the same vector in a packaging cell line would produce infectious virus particles and, depending on the nature of the disablement and insert sequences, may endow the GMM (the packaging cell line) with a phenotype likely to cause disease.

44 Examples of gene products which are not in themselves harmful, but may act in conjunction with the host's existing characteristics are: pathogenicity determinants (such as adhesion factors, penetration factors or surface components providing resistance or attachment to host defence mechanisms) or surface proteins that possess a receptor binding capacity which could alter colonisation ability or tissue tropism. Careful consideration should be given as to whether, within the context of the GMM, these determinants are likely to substitute for disabling mutations or act alongside existing pathogenicity determinants.

Gene transfer to other organisms

45 In all relevant cases, the ability of the vector to transfer sequences to other species should also be considered. The European Commission guidelines require that where it is known that a gene might be harmful in certain organisms but does not endow the actual GMM with a harmful phenotype, the vector and insert are not self-transmissible and are poorly mobilisable. Factors such as plasmid mobilisation or conjugation must be considered if it is possible that an insert gene which does not give rise to a harmful phenotype within a particular GMM could cause disease (or compromise treatment of disease) as a result of it being transferred by natural gene transfer processes to a different host organism. As in the discussion of indirect or remote effects on the environment (see Box 3), a degree of judgement will be needed about the probability and reasonable foreseeability of a vector transferring genes into another organism where they may result in disease in that organism or where they might enable it to cause disease or other harm to a further organism. For

plasmid vectors, further guidance can be found in HSE/ACGM guidance and 'poorly mobilisable' can be taken to be equivalent to the categories of 'non-mobilisable' and 'mobilisation defective'.

Example

As an example, the presence of a mobilisable or conjugative vector does not mean Group II status *per se*. Group II status would also not be appropriate for a harmless marker gene cloned on a broad host range conjugative vector. However, *Agrobacterium* Ti-genes on the same vector might result in a Group II GMM if it meant that introduced sequences encoding frost tolerance could be readily transferred to weed organisms where they might result in a phenotype with adverse effects on the environment.

46 As discussed in paragraphs 42 and 43, many complete proviral sequences in bacterial hosts are unlikely to be capable of producing infectious viral particles. Strictly speaking, this means that the viral DNA is unlikely to confer a hazardous phenotype on the bacteria. However, particular care must be taken over cases where intact proviral DNA is present, especially when it codes for serious pathogens, such as HIV or Hepatitus B virus. In such cases, even though there may be a low likelihood of harm from the GMM, this must be tempered by the extreme seriousness of the possible disease. In many cases full length proviral DNA sequences of such pathogens would warrant classification of their host bacterium as being equivalent to Group II.

Criterion iii: The genetically modified micro-organism is unlikely to cause disease to humans, animals or plants AND is unlikely to cause adverse effects on the environment

47 This criterion requires that the GMM as a whole is unlikely to cause disease and adverse effects on the environment (see Boxes 1 and 3). This stage should draw together the various components of the GMM as considered above and consider the hazards associated with the GMM itself. If both the recipient or parental micro-organism and the vector/ insert easily fulfil criteria (i) and (ii) respectively, the final GMM will probably comply with criterion (iii), but the GMM should still be carefully examined. For Type B operations the additional considerations in paragraphs 51 to 54 should be consulted.

48 Clearly, the most difficult cases will be those where the properties of the GMM mean that it is on the borderline between Group I and II. Particular attention should be given to the possibility of harm to the environment (Box 3), such as a harmful phenotype of another organism in the environment which resulted from gene transfer. Where there are any doubts it may be safest to assume that the final GMM is in Group II and to seek advice from HSE.

Other organisms which may be considered to be Group I

49 The European Commission guidelines also refer to one further class of organism which could be considered within Group I. This consists of GMMs **which are unlikely to cause disease to humans, animals or plants or to cause adverse effects on the environment** and which are constructed entirely from a single parental organism **or** consist of sequences from different species that exchange DNA by known physiological processes.

50 The Commission guidelines point out that GMMs in this category may fall under the definition of self-cloning (which is a technique that produces GMMs excluded from the Regulations if they belong to Group I) and any

GMM falling in this category may actually be excluded from the Regulations. The main difference to note is that self-cloning must involve sequences from **the same or phylogenetically closely-related species** that can **naturally** exchange genetic material with donor species, while this Group I classification criterion can involve **any** species that can exchange sequences by known physiological processes.

Additional considerations for organisms used in Type B operations

51 The European Commission guidelines include a number of additional considerations when GMMs are to be used in Type B operations:

(a) the vector and insert should not be self-transmissible and should be poorly mobilisable. Guidance on the interpretation of this can be found in paragraph 45. There is also a need to consider the presence of any functional transposing sequences, which might include transposon-based insertion vectors (if they retain all of the sequences associated with transposition) and active retroviral vectors as well as elements such as IS (insertional sequences) elements and proviral sequences that might be present in the cloned sequences;

(b) the vector and insert should also be limited in size and well characterised, but only to a degree sufficient to be able to confidently say that they are unlikely to endow the GMM with a harmful phenotype. If this is uncertain (for instance if the sequences are derived from a pathogen) it may be necessary to characterise further the sequences by considering the source and method of construction, or in some cases using techniques such as hybridisation or DNA sequencing. The construct may need to be modified to limit its size. Note that a detailed level of characterisation need not be done if it is possible to confirm *a priori* that the additional sequences will not result in a harmful phenotype.

Example

For example, a vector used in *Penicillium* which contains well characterised and harmless bacterial genes (marker genes or a replication origin) can be said to fulfil the requirement without further characterisation. Conversely, uncharacterised sequences downstream of the desired gene and derived from a source which could possibly contain harmful genes would need to be appropriately characterised (or the construct further modified to delete such sequences) if it were to be used as part of a Group I GMM in Type B operations.

52 For the final GMM to be used in Type B operations there are two further guidelines which should be considered. Firstly, the GMM should not be capable of transferring resistance genes to other micro-organisms **if it could compromise disease treatment**. Note that this consideration is dependent on the likelihood of transfer and on the type of antibiotic resistance gene involved.

Example

For example, a cloning vector for a large-scale bioremediation organism might be based on mercury resistance. Even if transfer were to occur to another organism it would not compromise disease treatment as mercury is not normally used to treat disease, although it is used in antimicrobials.

53 The second additional guideline is that the GMM should be as safe in the industrial setting as the parent organism **or** have characteristics that limit survival and gene transfer. This is intended to be a slightly more stringent threshold than applied to small-scale, Type A activities. If the GMM contains a vector/insert combination that fully meets all of the criteria above, it should be possible to conclude that the organism is as safe as the parent. Recognising that for some very low risk parent organisms, where almost any cloned sequences would make the GMM even fractionally less safe, the second part of the guideline allows the GMM to meet this requirement if there are built-in biological characteristics (biological barriers) which limit survival and gene transfer.

Example

For example, a plant growth hormone expressed from a wild-type *Bacillus subtilis* in Type B operation might be deemed to be marginally less safe in the industrial setting than the parent (even though unlikely to confer a phenotype which causes disease in plants) and therefore would be Group II. If, however, the parental organism was an auxotrophic or non-sporulating strain of *Bacillus*, and the vector was poorly mobilisable, then the GMM could be deemed to have biological characteristics that limit survival and gene transfer and be a Group I GMM.

54 It is important to note that such self-limiting characteristics may have already been present in the parental organism; they need not entail the further modification of the GMM. Appropriate biological characteristics which limit survival are commonly found in many micro-organisms that are adapted for large-scale or laboratory use; they include auxotrophy, sensitivity to UV light (*recA* mutations etc), non-sporulating strains and so on. They do not have to be artificial characteristics; even a 'wild-type' eukaryotic cell would have characteristics that limit survival. The considerations and examples of characteristics that limit gene transfer are indicated in paragraph 45.

Classification of organisms other than micro-organisms

55 Part II of Schedule 2 sets out the criteria for classification of higher organisms. The criteria are met when the particular GMO is not a micro-organism and when it is as safe in containment as the parental organism.

Example

For example, a cow producing human lactoferrin in its milk might be considered to be as safe in containment as the parental animal, whereas a mouse modified to express prion protein genes from a patient with Creutzfeld-Jacob disease might not.

Regulation 3

Application

(1) These Regulations shall have effect with a view to protecting persons against risks to their health, whether immediate or delayed, and for the protection of the environment, arising from activities involving genetically modified organisms.

(2) Regulations 8 to 12 shall not apply to the transport of genetically modified organisms by road, rail, inland waterway, sea or air.

(3) These Regulations shall not apply to the genetic modification of organisms

Regulation

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solely by any of the techniques referred to in Part III of Schedule 1 or to any organisms so modified.

(4) Insofar as these Regulations relate to the protection of the environment, they shall only apply to genetically modified micro-organisms.

(5) Nothing in these Regulations shall prejudice any requirement imposed by or under any enactment which relates to public health or the protection of the environment.

(6) These Regulations shall not extend to Northern Ireland.

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56 The Regulations apply both to risks to human health and the wider environment, and to all activities involving the contained use of genetically modified organisms with the following exceptions:

(a) the transport of genetically modified organisms is subject only to the requirements for risk assessment in regulation 7 and the provisions of regulation 13 onwards. In carrying out a risk assessment for transport, the parameters in Schedule 3 need be applied only as far as they are relevant to transport. The notification requirements in regulations 8 to 10 do not apply. Note, however, that the transport of GMOs may be subject to the provisions of the Carriage of Dangerous Goods by Road and Rail (Classification, Packaging and Labelling) Regulations 1994;

(b) the Regulations do not apply to GMOs produced solely through the techniques of genetic modification listed in Part III of Schedule 1. These techniques are excluded so long as the parental or recipient organism is not itself a genetically modified organism. Such techniques include:

(i) some self-cloning (see guidance to regulation 2);

(ii) the construction of somatic animal (including human) hybridomas, which can be interpreted as any cell produced by the fusion of a somatic cell and a lymphoma cell;

(iii) cell fusion of plant cells where the resulting organism could be produced using 'traditional breeding methods', interpreted as practices which use one or more of a number of methods, including physical and/or chemical means and control of physiological processes, which can lead to successful crosses between plants of the same botanical family.

57 These Regulations do not apply in Northern Ireland, which has separate but matching Regulations.

Regulation 4

Meaning of 'work' and 'at work'

Regulation

4

For the purpose of these Regulations and Part I of the Health and Safety at Work etc Act 1974[(a)] the meaning of "work" shall be extended to include any activity involving genetic modification and the meaning of "at work" shall be extended accordingly.

(a) 1974 c.37.

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58 This regulation extends the meaning of 'work' and 'at work' in the HSW Act so as to include all activities involving the contained use of genetically modified organisms, whether the person concerned is an employer, an

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employee, a self-employed person, or someone involved in genetic modification work who does not fall into one of these categories, such as a research student. All such activities are covered both by the general duties in Part I of the HSW Act and by the Contained Use Regulations.

Regulation 5

Modification of section 3(2) of the Health and Safety at Work etc Act 1974

Regulation

5

Section 3(2) of the Health and Safety at Work etc Act 1974 shall be modified in relation to an activity involving genetic modification so as to have effect as if the reference to a self-employed person therein is a reference to any person who is not an employer or an employee and the reference in it to his undertaking includes a reference to such an activity.

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59 This regulation modifies section 3(2) of the HSW Act, which requires self-employed persons to conduct their undertakings in such a way as to ensure, so far as is reasonably practicable, that people other than employees are not exposed to risks to their health and safety. Regulation 5 extends the meaning of 'self-employed person', in relation to an activity involving genetic modification, to anyone who is not an employer or an employee.

Regulation 6

Prohibition of certain work with genetically modified organisms outside containment

Regulation

6

(1) Subject to paragraph (2), any operation in which organisms are genetically modified or in which such genetically modified organisms are cultured, stored, used, transported, destroyed or disposed of is prohibited unless it is undertaken in conditions of contained use in accordance with these Regulations.

(2) Paragraph (1) shall not apply to any operation in which -

(a) genetically modified organisms are cultured, stored, used, transported, destroyed or disposed of, where such organisms are or are contained in -

(i) a product marketed in pursuance of either -

(aa) a consent granted by the Secretary of State under section 111(1) of the Environmental Protection Act 1990[(a)]; or

(bb) a written consent given by another competent authority of a member State in accordance with Article 13(4) of Council Directive 90/220/EEC[(b)] on the deliberate release into the environment of genetically modified organisms;

and in either case, the operation is conducted in accordance with any conditions or limitations attached to that consent, or

(ii) a medicinal product for human or veterinary use marketed in accordance with Council Regulation (EEC) No.2309/93[(c)]; and

(a) 1990 c.43.
(b) OJ No. L117, 8.5.90, p.15.
(c) OJ No. L214, 24.8.93, p.1.

Regulation

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(b) genetically modified organisms are released or marketed in circumstances in which the consent of the Secretary of State is required under section 111(1) of the Environmental Protection Act 1990.

(3) In this regulation, "product" means a product consisting of or containing a genetically modified organism or a combination of genetically modified organisms.

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60 Regulation 6 expresses the central requirement that for all work with GMOs the requirements of the Contained Use Regulations should be met, unless:

(a) the GMOs involved are, or are in, a product cleared for marketing under the Environmental Protection Act 1990, or under certain other product marketing legislation or European Community procedures, and the work does not involve further genetic modification unless specifically allowed by the consent conditions;

(b) the activity is a deliberate release or marketing of a GMO subject to section 111(1) of the Environmental Protection Act 1990 (in which case the consent of the Secretary of State should be obtained).

61 Some products may be sold without that clearance **on condition that** they are used under contained use conditions, and in such cases the Regulations apply in full. The mere fact that a GMO is, or is in, a bought product does not mean that it has been cleared for marketing under the legislation mentioned above.

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Regulation 7 Risk assessment

Regulation

(1) A person shall not -

(a) use any premises for activities involving genetic modification for the first time; or

(b) undertake any activity involving genetic modification,

unless he has ensured that, before commencing that use or activity, as the case may be, a suitable and sufficient assessment of the risks created thereby to human health and the environment has been made.

(2) Without prejudice to the generality of paragraph (1), the purposes of the assessment undertaken under that paragraph shall include -

(a) classifying any genetically modified organisms involved in the activity in accordance with the provisions of Schedule 2; and

(b) where appropriate, making decisions about the levels of containment required for the activity concerned.

(3) In making the assessment required by paragraph (1) the person undertaking that assessment shall -

(a) in particular, take due account of the parameters set out in Schedule 3 in as far as they are relevant; and

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Regulation

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(b) in a case in which the Executive has approved a method in relation to the activity involving genetic modification concerned or in relation to a particular element of that assessment, undertake the assessment in accordance with that method.

(4) The assessment shall be reviewed forthwith if -

(a) there is reason to suspect that the assessment is no longer valid; or

(b) there has been a significant change in the activity to which the assessment relates.

(5) The person making the assessment shall make a record of it and of any subsequent review and shall keep that record for at least 10 years from the date on which use of the premises or the activity, as the case may be, to which the assessment related, ceased.

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62 This regulation requires that a risk assessment for both human health and the environment, taking account of the parameters set out in Schedule 3 to the Regulations so far as they are relevant, must be made before any premises can be used for genetic modification activities or any such activities are undertaken. Rather than requiring the person undertaking the activities to actually carry out the risk assessment, regulation 7(1) requires that he or she has ensured that a suitable and sufficient risk assessment has been made. This has the effect of allowing a risk assessment undertaken by someone else to be adopted by the person wishing to carry out the work providing that that person is satisfied that it is adequate.

63 Under regulation 7(2), two of the purposes of the risk assessment are to classify the organisms involved, in accordance with Schedule 2 (see guidance to regulation 2), and make decisions about appropriate levels of containment (see also the guidance on regulation 12).

64 Risk assessments will vary in the amount of detail necessary to draw conclusions about the hazards of the activity, the likelihood that they will give rise to harm, and the control measures that are needed. Simple operations involving low hazard, well known and well understood organisms may normally need less detailed consideration than complex activities involving hazardous and less familiar organisms. For example it would be permissible to undertake a generic risk assessment covering work that involved a series of named *E. coli* K12 strains, whose disablement was well characterised, a series of named non-mobilisable vectors and a broadly defined type of insert. Any future work that fell within the boundaries set out for this generic assessment would then be covered and would not require reassessment unless there was a particular reason for doing so.

65 HSE/ACGM guidance on risk assessment includes work with prokaryotes, lower eukaryotes, eukaryotic viruses, plants and plant pests and animals.

66 HSE may approve a risk assessment method for particular activities or particular aspects of the assessment, and where it has done so, that method must be used. Any methods approved by HSE are likely to be based on HSE/ACGM guidance.

67 The Contained Use Regulations do not cover the environmental risks associated with the contained use of GMOs that are not micro-organisms - whole plants and animals for example. The contained use of large GMOs is, however, covered by section 108(1)(a) of the EP Act, which requires that

anyone who makes or obtains (the term 'acquire' in the Act embraces both these meanings) a GMO of this kind must make an assessment of the environmental risks. For this purpose section 108(1)(a) has been applied to the same range of genetic modification techniques as the Contained Use Regulations, and may be treated as an extension of them.* In practice, the assessment will normally be combined with the one required by regulation 7, and the same considerations should be taken into account. (Note that the Regulations do cover the human health risks associated with large GMOs, and for those risks the notification requirements in particular apply in the normal way.)

68 Under regulation 7(4), it is necessary to review the assessment where there is reason to suspect that the original assessment is no longer valid or where there has been a significant change in the activity to which the assessment relates. In this context significant change could include:

(a) change of scale of operation;

(b) change in containment conditions used;

(c) change of waste treatment procedures;

(d) new data on the behaviour of the organism, eg data on the toxicity of the gene product; on the level of gene expression; on the ability of the organism to cause harm in the environment etc.

69 Under regulation 7(5), records of risk assessments are required to be kept for at least 10 years from the date on which use of the premises or activity to which the assessment related has ceased. In practice, the very act of undertaking a risk assessment will usually generate a record of some sort. The record should be sufficient to serve two important purposes:

(a) to allow the persons involved in the activity to check the risk assessment and review it as necessary;

(b) to provide enforcing authority inspectors with a way of seeing what has been done in the past.

For similar reasons, records of environmental risk assessments relating to non-micro-organisms (animals and plants) must be kept for 10 years.

70 An adequate record will therefore contain facts and data and the conclusions of the risk assessment and the reasoning behind them. How much is needed on any particular point will depend on its importance in the assessment and the extent to which it is generally accepted material.

71 Under regulation 11, any persons undertaking a risk assessment (as opposed to ensuring that one has been undertaken - see paragraph 62) for the purposes of the Regulations must establish a genetic modification safety committee to advise them in relation to that assessment. See the guidance to regulation 11 for further information on such committees.

* This has been brought about by the Environmental Protection Act 1990 (Commencement No. 12) Order 1992 which activates section 108(1)(a) of the EP Act, and the Genetically Modified Organisms (Risk Assessment) (Records and Exemptions) Regulations 1996 (SI 1996/1106), which limit the application of section 108(1)(a) to the activities and risks described in paragraph 67 above.

Regulation 8

Notification of the intention to use premises for activities involving genetic modification for the first time

Regulation

(1) Subject to the following paragraphs of this regulation and regulation 10, no person shall undertake any activity involving genetic modification at any premises for the first time, unless he has notified the Executive of his intention to do so at least 90 days in advance or before such shorter time as the Executive may approve and with that notification has furnished the particulars specified in Schedule 4.

(2) In the case of activities involving the genetic modifications of micro-organisms, separate notifications shall be made of an intention to use the premises for activities involving genetically modified micro-organisms of Group I or Group II, except that a separate notification shall not be required -

(a) where a consent has already been given under paragraph (3) for activities involving Group II micro-organisms and the premises are to be used for activities involving Group I micro-organisms; or

(b) where simultaneous notification is being given of an intention to use premises for activities involving both Group I and Group II micro-organisms.

(3) In the case of activities involving genetically modified micro-organisms of Group II, the premises shall only be used for those activities after the Executive has given its consent.

(4) In any other case, the use of the premises for the activity may be commenced at or after the end of the period of 90 days or such shorter period as the Executive may have approved in pursuance of paragraph (1) unless the Executive objects in writing before the end of the relevant period.

(5) In any case in which a consent is required under paragraph (3), the Executive shall communicate its decision on the application in writing within 90 days after the application was received.

(6) Nothing in this regulation shall prevent a person from notifying under regulation 9 an individual activity which he intends to undertake in the premises at the same time as making a notification under this regulation; in such a case he shall not commence the activity except in accordance with the time periods specified in this regulation.

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72 Under both this regulation and regulation 9, notification is required by the person undertaking or intending to undertake the activity involving genetic modification. In practice, the 'person' will generally be a body such as a company, university or research institute.

73 Notification under regulation 8 is required when premises are to be used for the first time for activities involving genetic modification. The extent to which groups of premises (for example, different laboratories within the same research institution or university; geographically separate parts of an institute/company etc) may be subject of a single notification will depend largely on the way in which the management structure of the body making the notification is organised. Advice in individual cases can be obtained from HSE.

74 Notification is required at least 90 days in advance of any intended activities or later with the agreement of HSE. Under regulation 10(6), notification under regulation 8 must be made in a form approved by HSE and a model form for this purpose can be obtained free from HSE at the address given at paragraph 14. The information to be notified is specified in Schedule 4 to the Regulations.

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75 Where premises are to be used for the first time for activities involving micro-organisms, notifiers must indicate whether Group I or Group II micro-organisms or both are to be used. It is permissible to include activities with Group I and Group II micro-organisms in a single notification. Where a notification of intention to undertake activities involving Group I micro-organisms has been made and it is subsequently the intention to undertake activities involving Group II micro-organisms then a further notification is required. However, if a consent has been given for first use of Group II micro-organisms it is not necessary to make further notification under regulation 8 if it is then intended to begin activities involving Group I micro-organisms.

76 Notification requirements for both the premises (regulation 8) and the individual activities (regulation 9) must be met. For notifications under regulation 8, premises may be used for activities with Group I micro-organisms, or organisms other than micro-organisms, at the end of 90 days or sooner if HSE confirms that it does not object. For notification of intention to use premises for activities with Group II micro-organisms, the premises may be used only with the consent of HSE, which will be granted only with the agreement of the Secretary of State for the Environment (or Scotland or Wales) in relation to environmental protection. HSE will review notifications as quickly as possible, normally replying within about 30 days. In any case notifiers will be informed of the outcome of consideration of consent applications within 90 days of the receipt of the application. This time excludes any periods when HSE is awaiting additional information (see regulation 10(1)).

77 The regulation also provides that notification of intention to use premises for the first time under regulation 8 and notification of individual activities under regulation 9 can be submitted at the same time; under certain circumstances this could avoid duplication of information supplied - such as a summary of the risk assessment. The notifications will be considered together, with relevant time periods running concurrently. In accordance with regulation 8, individual activities, if notified at the same time as an intention to use premises for the first time, can only be commenced after a period of 90 days or sooner if HSE confirms that it does not object.

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Regulation 9

Notification of individual activities involving genetic modification

Regulation

(1) Subject to the following paragraphs of this regulation and regulation 10, no person shall undertake any activity involving genetic modification unless he has notified the Executive of his intention to do so at least 60 days in advance or before such shorter time as the Executive may approve and has furnished the particulars specified in the following paragraphs of this regulation and, except in the case of an activity to which paragraph (5) applies, the activity may be commenced after the expiry of the relevant period if by then the Executive has not objected in writing.

(2) In the case of an activity which is -

(a) a Type A operation involving only micro-organisms classified as Group I; or

(b) an activity involving genetically modified organisms other than micro-organisms and which satisfy the criteria set out in Part II of Schedule 2,

it shall be a sufficient compliance with paragraph (1) if the person undertaking the activity keeps a record of such activities and forthwith after the end of each calendar year notifies the Executive -

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Regulation

(i) of the total number of risk assessments under regulation 7 undertaken during that year;

(ii) where appropriate, that he is intending to continue to undertake such activities; and

(iii) that the information notified to the Executive in accordance with regulation 8 remains correct.

(3) In the case of an activity which is a Type B operation involving only micro-organisms classified as Group I, the specified particulars for the purposes of paragraph (1) shall be those specified in Part I of Schedule 5.

(4) In the case of an activity which is -

(a) a Type A operation involving genetically modified micro-organisms classified as Group II; or

(b) an activity involving genetically modified organisms other than micro-organisms and which do not satisfy the criteria set out in Part II of Schedule 2,

the specified particulars for the purposes of paragraph (1) shall be those specified in Parts I and II of Schedule 5.

(5) In the case of an activity which is a Type B operation involving genetically modified micro-organisms classified as Group II, the specified particulars for the purposes of paragraph (1) shall be those specified in Parts I, II and III of Schedule 5 and the activity shall only be commenced with the consent of the Executive.

(6) In any case in which a consent is required under paragraph (5), the Executive shall communicate its decision on the application in writing within 90 days after the application was received.

(7) The Executive may accept as a single notification a connected programme of work covering more than one activity involving genetic modification at one site, or a single activity carried on by the same person at more than one site.

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78 This regulation deals with notification of specific activities involving genetic modification. Under regulation 9(7), HSE may accept as a single notification a connected programme of work covering more than one activity. To be treated in this way the work covered by the notification should form a coherent and integrated programme. In order to satisfactorily meet these criteria a programme would normally be based around the study of a particular type of gene in a particular type of bacterial host/vector combination or eukaryotic virus. The scope of the work covered by the notification should be clearly defined so making it possible to identify the most hazardous insert and vector combination that will be used. In other words the notification should set out the factors which define the extent of the biological hazards and risks, ie set the boundaries of the work. For example a connected programme could involve the cloning of a series of named cytokines in *E. coli* and then going on to express them in disabled retroviruses, vaccinia and an E1-deleted adenovirus.

79 A notification should not simply cover everything that happens to be taking place on one site, since this would almost certainly lack any scientific coherence and make it extremely difficult to keep a track of the scope of the work as the research developed. Different phases or elements of a particular activity should be considered as part of the initial notification, which should cover all foreseeable aspects of the intended work. The same level of detail is required in the submission of a connected programme, as would be the case if

each individual element of the activity were to be notified independently. Clearly, however, it is not always possible to forecast or predict where a project might lead. If the direction of the project leads to work being proposed that will alter the risk assessment, there is a requirement to notify HSE in accordance with regulation 10(4).

80 Under regulation 10(6), notification under regulation 9 must be made in a form approved by HSE and model forms for this purpose can be obtained free from HSE at the address given in paragraph 14. The information to be notified, the time period for notification, and whether a consent is required depend on the nature of the activity and can be summarised as follows:

Type A operations involving Group I micro-organisms or operations involving organisms other than micro-organisms which satisfy the criteria in Part II of Schedule 2 - regulation 9(2)

In these cases, advance notification of individual activities is not required (but first-use notification under regulation 8 must still be given). Instead, records of activities need to be kept available for inspection. At the end of each calendar year HSE should be notified forthwith of:

(a) the total number of risk assessments required under regulation 7 undertaken during that year;

(b) whether the activities are to be continued; and

(c) changes to any particulars previously notified.

A model form for the annual retrospective return is available free from HSE at the address given in paragraph 14. (HSE will normally distribute these forms when the annual retrospective notification is due.)

Type B operations involving Group I micro-organisms - regulation 9(3)

The information specified in Part I of Schedule 5 should be notified 60 days in advance of the proposed activity, or later with the agreement of HSE. The activity may proceed at the end of the notification period provided that no objection is raised by HSE, and in accordance with any conditions imposed by HSE.

Note that the information submitted with Group I-Type B notifications should demonstrate that environmental harm will not be caused as a result of effluent discharge. If it does not so demonstrate then HSE is likely to ask for more information (see regulation 10). If the additional information provided indicates that contact of genetically modified micro-organisms with people or the environment is not sufficiently limited, HSE will object and the activity, as contained use, will not be permitted.

Type A operations involving Group II micro-organisms and operations involving organisms other than micro-organisms which do not satisfy the criteria in Part II of Schedule 2 - regulation 9(4)

The information specified in Parts I and II of Schedule 5 should be notified 60 days in advance of the proposed activity, or later with the agreement of HSE. The activity may proceed at the end of the notification period provided that no objection is raised by HSE, in accordance with any conditions imposed by HSE.

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Type B operations involving Group II micro-organisms - regulation 9(5)

The information specified in Parts I, II and III of Schedule 5 should be notified. The activity can proceed only with the consent of HSE. HSE will not grant a consent relating to environmental protection without the agreement of the Secretary of State. Notifiers will be informed of the outcome of their applications within 90 days from the date of receipt.

Regulation 10

Additional provisions relating to notifications and consents

Regulation

(1) Where necessary for the purpose of evaluating a notification made under regulation 8 or 9, the Executive may require in writing the person making the notification to give such additional information relating to the proposal as it may specify and in such a case the person making the notification shall not proceed with the activity involving genetic modification until the Executive gives its approval and the period between the time when the Executive requires the information and the notifier responds to the satisfaction of the Executive shall not be taken into account in calculating the periods of days referred to in the provisions concerned.

(2) Any consent granted by the Executive under regulation 8 or 9 may be granted subject to conditions or to a limit of time and may be revoked or varied at any time and in such a case the person undertaking the activity shall comply with those conditions.

(3) In so far as they relate to the protection of the environment, the Executive shall not grant, vary or revoke a consent under regulation 8 or 9, or give its approval under paragraph (1) without the agreement of the Secretary of State.

(4) Where a person making a notification in pursuance of regulation 8 or 9 subsequently makes a significant change in any premises or activity to which the notification relates or becomes aware of any new information which would affect the particulars previously notified, he shall forthwith notify the Executive thereof.

(5) If information subsequently becomes available to the Executive which could have significant consequences for the risks to health or the environment created by an activity involving genetic modification which has been notified to it, it may require the notifier to modify the conditions under which the activity is carried out, or to suspend or terminate the activity.

(6) Notifications made in pursuance of regulations 8 and 9 shall be in a form approved by the Executive.

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Guide

81 This regulation deals with:

(a) requests by HSE for additional information, which stop the clock as far as the specified time periods are concerned. When additional information is asked for, the activity may not be started until HSE has given its written approval, but note that this is quite separate from 'consent' as required by regulations 8(3) and 9(5);

(b) provision for conditions to be specified as part of a consent, or for a consent to be varied or revoked;

(c) the need for notification of any significant changes in premises or

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activities or new information which would affect the particulars previously notified. This is not in itself a new notification calling for the payment of a further fee, though it may lead to the variation or revocation of an existing consent or indicate that the work has changed sufficiently for a new full notification to be necessary. See paragraphs 78 and 79 for a discussion of connected programmes and what would constitute a reasonable scope. The same considerations would apply when judging if a regulation 10(4) notification is appropriate. Where the alteration of an activity or organism is a 'significant' change which therefore requires a new or revised risk assessment (see paragraph 68) a summary of the new assessment should be attached with the notification to HSE. For example, if work is being undertaken which utilises a replication defective viral vector, and experimental needs justify it being replaced with a replication competent system, this may significantly alter the risk and require a regulation 10(4) notification. Similarly, if a non-mobilisable plasmid was replaced with a self-transmissible plasmid, this may affect the environmental risk, and require a regulation 10(4) notification. Where there is any doubt, HSE should be consulted. HSE should also be informed of significant changes in notified personnel (eg biological safety officer) and to the notified premises. For instance, if the notified premises are to be significantly extended by the addition of another building (particularly if the additional premises are at a different location) it is important that HSE is informed. Cessation of work involving genetic modification should also be notified;

(d) provision for HSE to require modification, suspension or termination of activities in the light of new information; and

(e) the need to make notifications under regulations 8 and 9 in a form approved by HSE. Information about the approved forms is given in the guidance to regulations 8 and 9.

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Regulation 11

Establishment of a genetic modification safety committee

Regulation 11

A person who undertakes an assessment made for the purposes of regulation 7(1) shall establish a genetic modification safety committee to advise him in relation to that assessment.

Guide

82 The only **statutory** purpose of a genetic modification safety committee (GMSC) is to advise on risk assessments made in compliance with regulation 7. A particular safety committee may have other functions, advisory or representative, but they fall outside the scope of the Regulations.

83 Here, as elsewhere in the Regulations, a 'person' may be a body such as a company, university or research institute.

84 A GMSC does not itself have the duty to make a risk assessment, or any of the other duties placed by the Regulations on a person undertaking activities involving genetic modification.

85 In practice, someone will have to assess risk in order to comply with regulation 7 in almost all establishments carrying out activities involving genetic modification, and a GMSC will be required. There may be cases however where:

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Guide

(a) the activity in question is a minor one ancillary to a major activity carried out by another organisation (eg storage, freeze drying or irradiation of GMOs produced elsewhere, and which remain the property of the producer);

(b) a risk assessment is made by the other organisation to cover both the major and ancillary activities, with advice from its own GMSC;

(c) the risk assessment is made available to the secondary establishment where the ancillary activity is carried out.

In such cases a GMSC need not be set up in the secondary establishment (at least not for this particular activity alone), as the risk assessment is not undertaken there. But the person carrying out the activity should still satisfy himself or herself that the assessment is suitable and sufficient.

86 There are no hard and fast rules governing the make-up of a GMSC. However, it should have enough members, with sufficient depth and range of knowledge and experience to:

(a) understand the risks to both human health and the environment arising from the proposed activity, and the extent to which those risks are uncertain;

(b) judge the adequacy of the risk assessment made under regulation 7;

(c) where appropriate, test its emerging conclusions by discussion so that the advice given is genuinely that of a committee and not an individual.

87 More information on the possible constitution and functions of statutory GMSCs and similar committees is given in HSE/ACGM guidance.

88 The comments made by the GMSC are part of the information to be supplied with notifications made under regulations 8 and 9, and HSE will take them into account when considering its response.

89 Note that other sources of advice may also be necessary. Regulation 6 of the Management of Health and Safety at Work Regulations 1992 requires that employers appoint competent persons to assist them in complying with health and safety legislation. Where there is a sufficiently competent biological safety officer the employer may wish to appoint him or her for that purpose, as regards work with GMOs.

Regulation 12

Standards of occupational and environmental safety and containment

Regulation

12

(1) For any activity involving genetically modified micro-organisms of Group I, the principles of good microbiological practice and the following principles of good occupational safety and hygiene shall apply -

(a) to keep workplace and environmental exposure to any physical, chemical and biological agent adequately controlled;

(b) to exercise engineering control methods at source and to supplement these with appropriate personal protective clothing and equipment where necessary;

Regulation

(c) to test and maintain control measures and equipment;

(d) to test, when necessary, for the presence of viable process organisms outside the primary physical containment;

(e) to provide training of personnel; and

(f) to formulate and implement local rules for the safety of personnel.

(2) For the purpose of paragraph (1) "adequate" in relation to the control of an agent means adequate having regard only to the nature of the agent and the nature and degree of exposure to such an agent and "adequately" shall be construed accordingly.

(3) For any activities involving genetically modified micro-organisms of Group II in Type A operations, in addition to the principles set out in paragraph (1) the containment measures shall be determined by a method approved by the Executive.

(4) For any activities involving genetically modified micro-organisms of Group II in Type B operations, in addition to the principles set out in paragraph (1) the containment measures set out in Schedule 6 shall be applied at an appropriate level so as to ensure a high level of health and safety and environmental protection.

(5) For any activities involving genetically modified organisms other than micro-organisms, the principles set out in paragraph (1) shall be applied in as far as they are appropriate.

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Guide

90 For work with Group I micro-organisms, control measures must be taken in accordance with principles of good microbiological practice and good occupational safety and hygiene, as set out in regulation 12(1) and (2). These principles are intended to protect both human health and safety and the environment. Level 1 laboratory containment as defined in HSE/ACGM guidance on containment, when applied together with the principles of good occupational safety and hygiene, will normally be appropriate for work with Group I GMMs. This correspondence should not be assumed, however, and the classification of the GMM and the derivation of containment level should be carried out independently, but if the GMM classification is Group I and the assessed level of containment is higher than level 1 then both should be checked to make sure that they are correct. The HSE/ACGM guidance also deals with the safe operation of scale-up work.

91 For work with Group II micro-organisms in Type A operations, regulation 12(3) requires, in addition to observance of the above principles, containment measures, determined by a method approved by HSE. The approved method is the application at an appropriate level, based on the risk assessment, of the measures set out in the HSE/ACGM guidance on containment, which contains advice on safe systems of work. Four physical containment levels are defined, numbered 1 to 4 (B1 to B4 for large scale) in ascending order of thoroughness. All ACGM levels are in accordance with the principles of good microbiological practice.

92 Containment provisions to be used for work with Group II micro-organisms in Type B operations are set out in Schedule 6, at three levels: B2, B3 and B4. (These were previously in use under the 1989 Regulations for large-scale categories LS1, LS2 and LS3 and they are set out in HSE/ACGM guidance on large-scale work.)

93 For genetically modified organisms other than micro-organisms, the

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principles set out in regulation 12(1) must be applied as appropriate. HSE/ACGM guidance sets out standards for physical containment for work with transgenic animals and glasshouse work.

94 Certain GMOs may fall within the definition of 'biological agents' under the COSHH Regulations 1994. Under COSHH, the selection of control measures for biological agents is prescribed according to their risk to human health, while the Contained Use Regulations set out containment measures which must be selected at a level appropriate to the assessment of risks to both human health **and the environment.** Where there is a mismatch, the stricter requirements should be applied. This may arise, for example, for a genetically modified biological agent which presents a low risk of disease in humans but which is environmentally harmful; in which case, the risk management measures to ensure environmental protection must be applied.

Regulation 13

Emergency plans

Regulation

13

(1) Where the assessment made in accordance with regulation 7(1) shows that as a result of any reasonably foreseeable accident the health or safety of persons outside the premises in which an activity involving genetic modification is carried on is liable to be affected or there is a risk of damage to the environment, the person undertaking the activity shall ensure that a suitable emergency plan is prepared with a view to securing the health and safety of those persons and the protection of the environment.

(2) The person preparing the plan shall consult such persons, bodies and authorities as are appropriate and shall inform the emergency services in writing of the plan and of the hazards to which the plan relates.

(3) The person undertaking the activity involving genetic modification which is the subject of the emergency plans shall take appropriate measures to inform persons who are liable to be affected by an accident of the safety measures and the correct behaviour to adopt in the event of an accident.

(4) The information required to be given in pursuance of paragraph (3) shall be repeated and brought up to date at appropriate intervals and shall be made publicly available.

Guide

13

95 An emergency plan must be prepared if the risk assessment carried out under regulation 7(1) indicates that, as a result of any foreseeable accident, the health and safety of people outside the premises may be affected or if there is any risk to the environment. In practice, an emergency plan is unlikely to be necessary for any activities other than for Type B operations involving Group II micro-organisms.

96 Nevertheless, it is advisable for the emergency services to be informed of the nature of any potentially harmful organisms, even if the risk assessment indicates no potential for harm outside the premises, as this may affect their strategy in carrying out their duties. For example, fighting a fire at the premises may need special tactics as water used to extinguish it may carry organisms into the environment; emergency vehicles and other equipment may also need to be cleaned in a particular way to avoid transporting organisms outside the site; or the police may need to follow special procedures if the premises are burgled.

97 Where an emergency plan is produced, it should be a written document, kept up to date to reflect changes in risk procedures and personnel. Anyone on the site who is affected by the plan should be aware of its relevant provisions;

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not only people who may have duties under it but also those who may need to be evacuated from the site in an emergency, including contractors and visitors. The plan should be drawn up in consultation with appropriate organisations including the emergency services (fire, police and ambulance), the local authority emergency planning officer and Environmental Health Department, and relevant parts of the health service network. In England and Wales the plan should also be brought to the attention of the National Rivers Authority and the company appointed for the local water supply, and in Scotland the appropriate water authority, and the Scottish Environment Protection Agency which is responsible for the control of environmental pollution.

98 Examples of information which could be recorded in an emergency plan include:

(a) the types of incidents to people or the environment to be taken into account and the immediate steps to be taken;

(b) organisations involved, including key personnel, their responsibilities and liaison arrangements between them;

(c) communication links including arrangements for giving information to people liable to be affected by any accident and for making such information publicly available;

(d) special equipment, including damage control and repair items;

(e) technical information such as the nature of the organism, characteristics of the plant and other hazards which may be present;

(f) information about the site including likely locations of personnel and hazardous organisms;

(g) evacuation arrangements;

(h) contacts and arrangements for obtaining further advice and assistance, eg meteorological information, medical services, water and agricultural authorities;

(i) arrangements for dealing with the media;

(j) longer-term clean-up.

99 Steps to make the information in the emergency plan publicly available should be taken in consultation with the local authority, which may be able to offer advice and assistance with the provision of public information, for example by allowing information to be placed in public buildings such as libraries, civic centres and town halls.

13

Regulation 14

Notification of accidents

Regulation

14

(1) Where an accident occurs, the person undertaking the activity involving genetically modified organisms shall forthwith notify the Executive of it and shall provide the following information -

(a) the circumstances of the accident;

(b) the identity and quantity of genetically modified organisms released;

Regulation

14

(c) any information necessary to assess the effects of the accident on the health of the general population and on the environment; and

(d) the emergency measures taken.

(2) Where the Executive receives a notification in pursuance of paragraph (1), the Executive shall -

(a) ensure that any emergency, medium and long term measures are taken;

(b) immediately inform any other member State that could be affected by the accident;

(c) collect, where possible, the information necessary for a full analysis of the accident and, where appropriate, make recommendations to avoid similar accidents in the future and to limit their effects; and

(d) send to the European Commission the information provided for under paragraph (1), together with an analysis of the accident and details of any recommendations made to avoid similar accidents in the future and to limit their effects.

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100 This regulation requires immediate notification to HSE of any accident, defined in regulation 2 as any incident involving a significant and unintended release of GMOs which presents a hazard, immediate or delayed, to either human health and safety or to the environment.

101 Spillages of Group I micro-organisms are unlikely to count as significant releases of genetically modified organisms which present hazards, and they will not routinely require notification. This may not be true, however, for spillages of Group II micro-organisms.

102 In accordance with guidelines agreed by member States of the European Union, the information should be set out as in Appendix 3.

103 Accident notifications should be sent to:

Health and Safety Executive
Division of Science and Technology, E4
Magdalen House
Stanley Precinct
Bootle
Merseyside L20 3QZ
Tel: 0151 951 4831
Fax: 0151 922 7918

Regulation 15

Disclosure of information notified

Regulation

15

(1) Information notified in pursuance of regulations 8 to 10 shall not be treated as relevant information for the purposes of section 28 of the Health and Safety at Work etc Act 1974.

(2) Where a person making a notification in pursuance of regulations 8 to 10 indicates that it contains certain information the disclosure of which might harm his competitive position and should be kept confidential, full justification for that indication shall be given and in such a case after consulting the notifier the Executive shall decide which information shall be kept confidential and shall inform the notifier of its decision.

Regulation

(3) Nothing in paragraph (2) shall apply to the following information which shall not be kept confidential -

(a) the name and address of the notifier and the location of the activity involving genetic modification;

(b) the purpose of the activity;

(c) the description of the genetically modified organism involved;

(d) methods and plans for monitoring the genetically modified organism and for emergency response; and

(e) the evaluation of foreseeable effects and in particular pathogenic effects and ecologically disruptive effects.

(4) Notwithstanding paragraph (3), where the Executive is satisfied on the basis of detailed evidence submitted to it by the notifier and where appropriate, after consultation with the notifier, that it is necessary to withhold, for the time being, certain of the information specified in paragraph (3) in order to protect his intellectual property rights, the Executive shall withhold that information to the extent and for so long as it is necessary to protect those rights.

(5) Information which is kept confidential in accordance with paragraph (2) or withheld in accordance with paragraph (4) shall be disclosed only -

(a) to the Secretary of State;

(b) to the European Commission or the competent authority for Northern Ireland or another member State;

(c) for the purpose of any legal proceedings;

(d) with the consent of the notifier; or

(e) to the extent necessary to evaluate the notification.

(6) A person who receives information in accordance with sub-paragraph (e) of paragraph (5) shall not use that information except for a purpose of the Executive or the Secretary of State.

(7) Where the notifier has requested that certain information in the notification shall be kept confidential in accordance with paragraph (2) or withheld in accordance with paragraph (4), the Executive shall not disclose any of that information (except in accordance with paragraph (5)) until at least 14 days after it has reached a decision under the relevant paragraph.

(8) After consulting the notifier, the Executive may review any decision made under paragraph (2) or (4) and shall inform the notifier of the result of that review.

(9) Where, for whatever reason, the notifier withdraws the notification, the Executive shall not thereafter disclose any of the information supplied.

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Guide

104 This regulation determines whether HSE may disclose the information submitted as part of a notification or must withhold it. The regulation begins by disapplying section 28 of the HSW Act, so that the information submitted is not subject to the disclosure restrictions imposed by that section. It goes on to specify new restrictions to cover the case of a GMO notification.

105 For any of the information submitted **except the items listed in regulation 15(3)** the notifier may ask that it should be kept confidential, on the grounds that disclosure would harm his or her competitive position. If HSE accepts the claim, which must be supported by a full justification, the

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Guide

information in question will not be disclosed. Separately, the notifier may ask that any of the information covered by regulation 15(3) should be withheld if disclosure would damage his or her intellectual property rights. This includes damage to the future patentability of an invention, and notifiers who are in doubt about the effect of disclosure on future patents are strongly advised to seek professional advice before making their notification. Again, a full and detailed justification must be given to support a request of this kind. Where the justification depends to some degree on the protection of patentability it should preferably be supported by evidence based on the opinion of a patent agent.

106 The status of information which HSE agrees not to disclose for either of the reasons set out above will be reviewed at intervals, and if the grounds for withholding it have disappeared then it will become disclosable. An argument that absolutely everything covered by regulation 15(3) should be withheld will not succeed: it should be assumed that some information, if necessary in broad and general terms, can always be disclosed. Whenever a case is being made for non-disclosure, the notifier should indicate at the same time the nature of the information which **could** be disclosed without harm to his or her interests. The identity of the notifier, however, will be disclosed only as the name of the organisation or corporate body carrying out the work. The names of individual persons will not be revealed.

107 If notifiers are in doubt about the application to them of these parts of the Regulations, and to avoid later delays during the processing of the notification itself, they may find it helpful to discuss their proposals confidentially and informally with HSE officials before submitting their notifications.

108 Some limited disclosure will always be necessary to meet HSE's statutory obligations and so that the notification can be evaluated. This is provided for in regulation 15(5). Information may be given in particular to members of ACGM, whose opinion will be taken into account by HSE in its decisions on consent or objection. Anyone receiving information in this way may not use it except for the purpose for which it was given.

109 If at any time a notifier withdraws a notification, disclosure of any information associated with it will cease, though of course by that time some of it may already be in the public domain. But information which the notifier has asked HSE to withhold will not be disclosed until the notifier's case has been assessed and a decision reached, and if necessary the notifier has been given the opportunity to withdraw the notification.

Regulation 16

Register of notifications

Regulation

(1) The Executive shall maintain a register of notifications to which regulation 8(3) or 9(5) relate (for which the consent of the Executive is required) and that register shall be open to inspection by members of the public at any reasonable time.

(2) The register referred to in paragraph (1) shall contain in relation to each such notification -

(a) such of the information referred to in regulation 15(3) as has not been withheld in accordance with paragraph (4) of that regulation; and

(b) a statement as to whether or not the consent of the Executive has been granted.

(3) The information referred to in sub-paragraph (a) of paragraph (2) shall be entered in the register within 14 days of its receipt by the Executive and the

Regulation

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information referred to in sub-paragraph (b) of that paragraph within 14 days of the decision whether or not to grant the consent having been made, except that where the notifier has requested that certain information specified in regulation 15(3) be withheld in accordance with regulation 15(4), that information shall only be entered in the register not less than 14 days but not more than 28 days after the Executive has made a decision not to withhold that information.

(4) Copies of the register shall be maintained at -

(a) the area office of the Executive in whose area the notifier is situated;

(b) Rose Court, 2 Southwark Bridge, London SE1 9HS; and

(c) Magdalen House, Stanley Precinct, Bootle, Merseyside L20 3QZ.

Guide

110 This regulation requires HSE to maintain a public register of notifications requiring consent (ie notifications of intention to use premises for activities involving Group II micro-organisms for the first time and individual Type B operations involving Group II micro-organisms). The information to be placed on the register is that specified by regulation 15(3); that is, the information for which a case for confidentiality may not be made on competitiveness grounds, but any of it which HSE has agreed to withhold under regulation 15(4), to protect the notifier's intellectual property rights, will not be placed on the register. Information subject to a request for non-disclosure will not be placed on the register while the request is being considered, and if HSE does not accept the case being made, until the notifier has been given the opportunity to withdraw the notification.

111 The approved notification form for consent applications contains a separate section for the register information. To avoid delay arising from inadequate proposed entries, notifiers should provide in this section as full and precise a description as possible of the organism, the purpose of the activity and the evaluation of foreseeable effects on human health and the environment, subject to the considerations set out in the guidance on regulation 15. It should summarise the information contained in the main notification document in sufficient detail to enable a user of the register to make an informed judgement about possible risks to the public and the environment.

112 Copies of the register are maintained at the area office of HSE in whose area the notifier is situated (addresses of HSE's local offices are given in general telephone directories under 'Health and Safety Executive') and at head offices of HSE. The head office addresses are:

Health and Safety Executive
Health Directorate, Division B2
Rose Court
2 Southwark Bridge
London SE1 9HS
Tel: 0171 717 6297/6348 Fax: 0171 717 6199

and

Health and Safety Executive
Division of Science and Technology , E4
Magdalen House
Stanley Precinct
Bootle
Merseyside L20 3QZ
Tel: 0151 951 4831 Fax: 0151 951 3474

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Registers are open to inspection by members of the public during normal office hours but those wishing to inspect them are advised to telephone first.

Regulation 17

Duties on receiving notifications

Regulation

17

The Executive shall examine a notification under regulation 8 or 9 for -

(a) the conformity with the requirements of these Regulations;

(b) the accuracy and completeness of the information given;

(c) the correctness of the classification of the organisms to which the notification relates in accordance with Schedule 2; and

(d) where appropriate, the adequacy of the waste management, safety and emergency response measures.

Regulation 18

Information to be sent to the Secretary of State

Regulation

18

Forthwith after receipt, the Executive shall send to the Secretary of State a copy in each case of -

(a) any notification received under regulation 8 or 9;

(b) any requirement for further information under regulation 10(1) and the response thereto; and

(c) any notification relating to an accident under regulation 14,

and if requested to do so by the Secretary of State shall require additional information under regulation 10(1).

Regulation 19

Reports to the European Commission

Regulation

19

The Executive shall send to the European Commission reports of notifications for which a consent is required under regulation 9(5) and summary reports of the application of these Regulations in accordance with Article 18 of the contained use Directive.

Guide

113 Under Article 18 of the Contained Use directive (90/219/EEC), member States are required to send to the Commission summary reports of notifications of individual activities for which a consent is required, ie Type B operations involving Group II organisms. These reports include the description, proposed uses and risks of the micro-organisms. In addition, every 3 years, member States are required to submit a report on their experience of the operation of the Directive. The Commission publishes a summary based on these reports.

Regulation 20

Exemption certificates

Regulation

20

(1) Subject to paragraph (2) and to any provisions imposed by the Communities in respect of the control and regulation of genetically modified organisms, the Executive may, with the agreement of the Secretary of State in so far as the

Regulation

20

exemption relates to the environment, by a certificate in writing, exempt any person or class of persons, genetically modified organism or class of genetically modified organisms from all or any of the requirements or prohibitions imposed by these Regulations and any such exemption may be granted subject to conditions and to a limit of time and may be revoked by a certificate in writing at any time.

(2) The Executive shall not grant any such exemption unless, having regard to the circumstances of the case and in particular to -

(a) the conditions, if any, that it proposes to attach to the exemption; and

(b) any requirements imposed by or under any enactments which apply to the case, it is satisfied that the health and safety of persons who are likely to be affected by the exemption or the protection of the environment will not be prejudiced in consequence of it.

Guide

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114 This regulation sets out the powers of HSE to make exemptions from the requirements of the Regulations. Before making any such exemption, HSE will consider the circumstances of the case and will need to be satisfied that the health and safety of people and the protection of the environment will not be prejudiced by it. Exemptions will also be subject to any provisions imposed by the European Communities in respect of the control and regulation of genetically modified organisms.

Regulation 21 Enforcement and civil liability

Regulation

21

(1) Insofar as any provision of regulations 6 to 14 is made under section 2 of the European Communities Act 1972[(a)] -

(a) the provisions of the Health and Safety at Work etc Act 1974 relating to enforcement and offences shall apply to that provision as if that provision had been made under section 15 of that Act; and

(b) in the event of a breach of duty imposed by that provision, it shall confer a right of action in civil proceedings if that breach of duty causes damage.

(2) Notwithstanding regulation 3 of the Health and Safety (Enforcing Authority) Regulations 1989,[(b)] the enforcing authority for these Regulations shall be the Executive.

(a) 1972 c.68.
(b) SI 1989/1903.

Guide

21

115 The effect of regulation 21(1) is that the provisions of these Regulations made under the European Communities Act 1972, including provisions in relation to the protection of the environment, are treated as if they were made under the HSW Act. The provisions of the HSW Act in relation to matters such as enforcement and serving of notices therefore apply, and rights of action in civil proceedings are conferred, as in the case of regulations made under the HSW Act.

116 Under regulation 21(2) HSE is the enforcing authority for the Contained Use Regulations in respect of both human health and environmental protection in all premises concerned, including those where local authorities enforce other HSW Act regulations.

Regulation 22

Fees for notifications

Regulation

22

(1) Fees shall be payable in accordance with paragraph (2) by a notifier to the Executive in relation to any matter referred to in that paragraph.

(2) The fees referred to in paragraph (1) shall be -

(a) subject to sub-paragraph (b), on each notification of the intention to use premises for activities involving genetic modification for the first time under regulation 8, £100;

(b) on each notification of the intention to use premises for activities involving genetic modification for the first time, where a consent is required under regulation 8(3), £130;

(c) subject to sub-paragraph (d), on each notification of individual activities involving genetic modification under regulation 9, £180;

(d) on each notification of individual activities involving genetic modification for which a consent is required under regulation 9(5), £270.

(3) This regulation shall not apply to any notification made for the purposes of regulation 23(1) or (3) (which relates to transitional provisions).

Guide

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117 A fee is charged to cover the cost of processing all notifications except the annual retrospective summaries permitted by regulation 9(2). There is a fixed scale of charges with four different fees in it: the one to be paid depends upon the type of notification being made. Payment should be made when the notification is submitted. Cheques should be made payable to 'Health and Safety Executive'. **NOTE: The scale of charges is updated annually, and notifiers should check with HSE if they are unsure what the current rates are.**

118 Where a simultaneous notification of first use of Group I and Group II GMMs is made (as allowed by regulation 8(2)(b)), the fee is that required for first use where a consent is required.

119 Where a notification covers a connected programme of work covering more than one activity, as permitted by regulation 9(7), only one fee is required, however many separate activities it includes.

Regulation 23

Transitional provisions

Regulation

23

(1) Where before 1 February 1993 a person had notified the Executive of his intention to undertake activities involving genetic modification which complied with regulation 5(1) and (2)(a) of the 1989 Regulations as then in force, that notification shall be treated as satisfying the requirements of regulation 8 except that regulation 8(3) shall apply to that activity on or after 1 February 1994.

(2) Before 2 May 1993 it shall be a sufficient compliance with regulation 8 if the notifier commences the activity having notified his intention to do so 30 days in advance or such shorter time in advance as the Executive may approve and regulation 8(3) shall not apply to activities commenced before 2 May 1993 until 1 February 1994.

(3) Where before 1 February 1993 a person had notified the Executive of his

Regulation

23

intention to undertake activities involving genetic modification which complied with regulation 5(1) and (2)(b) of the 1989 Regulations as then in force, that notification shall be treated as satisfying the requirements of regulation 9 except that regulation 9(5) shall apply to that activity on or after 1 February 1994.

(4) Before 2 April 1993 it shall be a sufficient compliance with regulation 9 if the notifier of an activity involving genetic modification had notified it in accordance with that regulation 30 days in advance or such shorter time in advance as the Executive may approve and regulation 9(5) shall not apply to activities commenced before 2 April 1993 until 1 February 1994.

(5) Regulation 10 shall apply to any notification made on or after 1 February 1993.

Guide

120 The transitional provisions expired on 1 February 1994. They ensured that those who had notified under the Genetic Manipulation Regulations 1989 could continue working, but also that those activities notified under the 1989 Regulations now subject to consent were brought within the new regime. Consents should now be held for all premises used for work involving Group II organisms, or for individual activities involving Group II organisms in Type B operations.

Regulation 24 Extension outside Great Britain

Regulation

24

These Regulations shall apply in relation to premises and activities outside Great Britain to which sections 1 to 59 and 80 to 82 of the Health and Safety at Work etc. Act 1974 apply by virtue of the Health and Safety at Work etc. Act 1974 (Application Outside Great Britain) Order 1989[a] as they apply to premises and activities within Great Britain.

(a) SI 1989/840.

Guide

121 The Regulations apply to premises and activities specified in the Health and Safety at Work etc Act 1974 (Application Outside Great Britain) Order 1989. Notification is therefore required of any activity which takes place on an offshore installation which is in territorial waters or areas designated under the Continental Shelf Act 1964, including the British North Sea oil fields. The Order, and therefore the Regulations, does not, however, apply to vessels in, or aircraft flying over, territorial waters or designated areas.

Regulation 25 Revocation

Regulation
25

The 1989 Regulations are revoked.

Schedule 1

Definition of genetic modification

Schedule

Regulations 2(1) and 3(3)

Part I Examples of techniques constituting genetic modification

1 Examples of the techniques which constitute genetic modification which are referred to in sub-paragraph (a) of the definition of genetic modification in regulation 2(1) are -

(a) recombinant DNA techniques consisting of the formation of new combinations of genetic material by the insertion of nucleic acid molecules, produced by whatever means outside the cell, into any virus, bacterial plasmid or other vector system so as to allow their incorporation into a host organism in which they do not occur naturally but in which they are capable of continued propagation;

(b) techniques involving the direct introduction into an organism of heritable material prepared outside the organism including micro-injection, macro-injection and micro-encapsulation; and

(c) cell fusion (including protoplast fusion) or hybridization techniques where live cells with new combinations of heritable genetic material are formed through the fusion of two or more cells by means of methods that do not occur naturally.

Part II Techniques which are not considered to result in genetic modification

2 The following techniques are not considered to result in genetic modification if they do not involve the use of recombinant-DNA molecules or genetically modified organisms -

(a) in vitro fertilisation;

(b) conjugation, transduction, transformation or any other natural process; and

(c) polyploidy induction.

Part III Techniques to which these Regulations do not apply

3 These Regulations shall not apply to the following techniques of genetic modification if they do not involve the use of genetically modified organisms as recipient or parental organisms -

(a) mutagenesis;

(b) the construction and use of somatic hybridoma cells (for example for the production of monoclonal antibodies);

(c) cell fusion (including protoplast fusion) of plant cells where the resulting organisms can also be produced by traditional breeding methods;

(d) self-cloning of non-pathogenic naturally occurring micro-organisms which fulfil the criteria of Group I for recipient micro-organisms; and

(e) self-cloning of non-pathogenic naturally occurring organisms other than micro-organisms which satisfy the criteria of Part II.

1

Schedule 2

Criteria for the classification of organisms

Schedule

2

Regulation 2(2)

Part I Criteria for the classification of genetically modified micro-organisms into Group I

A genetically modified micro-organism is classified into Group I when all of the following criteria are satisfied -

(1) The recipient or parental micro-organism is unlikely to cause disease to humans, animals or plants;

(2) The nature of the vector and the insert is such that they do not endow the genetically modified micro-organism with a phenotype likely to cause disease to humans, animals or plants, or likely to cause adverse effects in the environment;

(3) The genetically modified micro-organism is unlikely to cause disease to humans, animals or plants and is unlikely to cause adverse effects in the environment.

Part II Criteria for the classification of organisms other than micro-organisms

An organism which satisfies the criteria of this Part is a genetically modified organism -

(a) which is not a micro-organism; and

(b) which is as safe in the containment facility as any recipient or parental organism.

Schedule 3

Parameters to be taken into account in risk assessments, as far as they are relevant, under regulation 7

Schedule

3

Regulation 7(3)

Characteristics of the donor, recipient or (where appropriate) parental organism

1 The following matters shall be investigated and assessed in relation to any organism which is or will be a donor, recipient or parental organism -

(a) the name, species, subspecies and strain of the organism;

(b) the degree of relatedness between the donor, recipient (and where appropriate the parental) organism in relation to which the assessment is being carried out;

(c) the sources of the organism;

(d) the reproductive cycle of the organism;

(e) history of prior genetic modifications to the organism;

(f) the stability of the genetic traits of the organism;

(g) the nature of the pathogenicity, virulence, infectivity, toxicity, and vectors of disease transmission of the organism;

(h) the base sequence, frequency of mobilisation and specificity of the organism's indigenous vectors;

(i) the presence in the organism of genes which confer resistance;

(j) the host range of an organism which is a parasite or pathogen;

(k) the organism's other potentially significant physiological traits, and the stability of those traits;

(l) the organism's natural habitat and geographic distribution;

(m) the climatic characteristics of the organism's natural habitat;

(n) the significant involvement of the organism in environmental processes, including nitrogen fixation and pH regulation;

(o) the interaction of the organism with other organisms in the environment and its effect on those organisms, including its likely competitive or symbiotic properties;

(p) the ability of the organism to form survival structures, including seeds, spores or sclerotia.

Characteristics of the modified organism

2 The following matters shall be investigated and assessed in relation to an organism in relation to which a risk assessment under regulation 7 is carried out -

(a) the description of the modification, including the technique used or proposed to be used to introduce a vector or insert into the organism;

(b) the nature and source of the vector introduced into the organism;

(c) the function of the genetic modification and/or of the new nucleic acid;

(d) the structure and amount of any vector or donor nucleic acid remaining in the final construction of the modified organism;

(e) the stability of the genetic traits introduced into the organism;

(f) the frequency of mobilisation of inserted vector or genetic transfer capability;

(g) the rate and level of expression of the new genetic material in the organism, and the method and sensitivity of measurement of that rate and level;

(h) the activity of the expressed protein.

Health considerations

3 The following matters shall be investigated and assessed in relation to an organism in relation to which a risk assessment under regulation 7 is carried out -

(a) toxic or allergenic effects of non-viable organisms and/or their metabolic products;

Schedule

(b) product hazards;

(c) comparison of the modified micro-organism to the donor, recipient or (where appropriate) parental organism regarding pathogenicity;

(d) capacity for colonisation;

(e) if the organism is pathogenic to humans who are immunocompetent -

(i) diseases caused and mechanism of pathogenicity including invasiveness and virulence,

(ii) communicability,

(iii) infective dose,

(iv) host range, possibility of alteration,

(v) possibility of survival outside of human host,

(vi) presence of vectors or means of dissemination,

(vii) biological stability,

(viii) antibiotic-resistance patterns,

(ix) allergenicity,

(x) availability of appropriate therapies.

Environmental considerations

4 The following matters shall also be investigated and assessed in relation to an organism in relation to which a risk assessment under regulation 7 is carried out -

(a) the factors affecting survival, multiplication and dissemination of the modified organism in the environment;

(b) the available techniques for detection, identification, and monitoring of the modified organism in the environment;

(c) the available techniques for detecting transfer of the new genetic material to other organisms;

(d) the known and predicted habitats of the modified organism;

(e) the ecosystems to which the modified organism could be disseminated as a result of an escape;

(f) the anticipated mechanism and result of interaction between the modified organism and the organisms which might be exposed in case of the escape of the organism;

(g) the known or predicted effects of the organism on plants and animals, including pathogenicity, infectivity, toxicity, virulence, vector or pathogen allergenicity, colonisation, predation, parasitism, symbiosis and competition;

(h) the known or predicted involvement of the organism in biogeochemical processes, including nitrogen fixation and pH regulation;

(i) the availability of methods for decontamination of the area in case of release to the environment.

3

Schedule 4

Information required for a notification under regulation 8(1)

Schedule

Regulation 8(1)

1 A notification required for the purposes of regulation 8(1) shall include the following information -

(a) the name and address of the person responsible for carrying out the activity and the names of persons responsible for supervision, monitoring and safety together with details of their training and qualifications;

(b) address of the premises where the activity is to be carried on and its grid reference and, where appropriate, a description of the sections of the installation;

(c) a description of the nature of the activity to be undertaken, the likely scale of the operation and in particular, in the case of micro-organisms, their classification (whether in Group I or Group II);

(d) a summary of the risk assessment undertaken in accordance with regulation 7;

(e) the names and capacities of the members of the genetic modification safety committee;

(f) comments made by the genetic modification safety committee on the local arrangements for risk assessment;

(g) the names of the biological and deputy biological safety officers concerned with the intended activities (if any);

(h) the name of the supervisory medical officer (if any);

(i) the arrangements for health surveillance (if any); and

(j) any other information the Executive needs for the purpose of maintaining the register referred to in regulation 16.

4

Schedule 5

Information required for a notification under regulation 9

Schedule

Regulation 9

Part I Information required under regulation 9(3)

1 A notification required for the purposes of regulation 9(3) shall include the following information -

(a) the name and address of the person responsible for carrying out the activity;

(b) address of the premises where the activity is to be carried out;

(c) the date of the notification referred to in regulation 8(1);

(d) the parental organism used, or where applicable the host-vector system used;

(e) the source and the intended function of the genetic material involved in the modification;

5

(f) the identity and characteristics of the genetically modified organism;

(g) the purpose of the activity including the expected results;

(h) where appropriate the culture volumes to be used or the scale of the activity;

(i) details of waste treatment including levels of live genetically modified micro-organisms in the waste; and

(j) a summary of the risk assessment required in accordance with regulation 7 and of the comments of the genetic modification safety committee on it.

Part II Additional information required under regulation 9(4)

2 In addition to the information required under Part I a notification made for the purposes of regulation 9(4) shall contain the following information -

(a) a description of the sections of the installation involved and the methods for handling the organisms;

(b) a description of the predominant meteorological conditions and the potential sources of danger arising from the location of the installation;

(c) a description of the protective and supervisory methods to be applied throughout the duration of the activity; and

(d) in the case of micro-organisms, the containment level to which the micro-organism has been allocated in accordance with the risk assessment made in accordance with regulation 7(1) and in any case the safety precautions to be observed.

Part III Additional information required under regulation 9(5)

3 In addition to the information required under Parts I and II a notification made for the purposes of regulation 9(5) shall contain the information specified in paragraph 5.

4 If it is not technically possible, or if it does not appear necessary to give the information specified in paragraph 5, the reason shall be stated. The level of detail required in response to each subset of considerations is likely to vary according to the nature and scale of the proposed activity. In the case of information already submitted to the Executive by the notifier under these Regulations (or the 1989 Regulations) reference can be made to that information by him.

5 The additional information required is -

(a) information about the genetically modified micro-organisms -

(i) the identity and characteristics of the genetically modified micro-organisms,

(ii) the purpose of the contained use or the nature of the product,

(iii) the host-vector system to be used where applicable,

(iv) the culture volume to be used,

(v) behaviour and characteristics of the micro-organisms in the case of changes in the conditions of containment or release into the environment,

Schedule

5

(vi) overview of the potential hazards associated with the release of the micro-organisms into the environment, and

(vii) substances which are or may be produced in the course of use of the micro-organisms other than the intended product;

(b) information about personnel -

(i) the maximum number of persons working in the installation, and

(ii) the number of persons who will work directly with the micro-organisms;

(c) information about the installation -

(i) the activity in which the micro-organisms are to be used,

(ii) the technological processes used,

(iii) a description of the sections of the installation involved, and

(iv) the predominant meteorological conditions and specific hazards arising from the location of the installation;

(d) information about waste management -

(i) types, quantities and potential hazards arising from the use of the micro-organisms,

(ii) waste management techniques used including recovery of liquid or solid wastes and the inactivation techniques used, and

(iii) ultimate form and destination of inactivated wastes;

(e) information about accident prevention and emergency response plans -

(i) the sources of hazards and conditions under which accidents might occur,

(ii) the preventive measures applied such as safety equipment, alarm systems, containment methods and procedures and available resources,

(iii) a description of information given to workers, and

(iv) the information necessary for the Executive to evaluate any emergency plan prepared in accordance with regulation 13;

(f) the full risk assessment referred to in regulation 7; and

(g) any other information the Executive needs for the purpose of maintaining the register referred to in regulation 16.

Schedule 6

Containment measures for micro-organisms of Group II

Schedule

Regulation 12(4)

1 The containment measures for Type B operations using micro-organisms from Group II shall be chosen by the user from the levels in the table below as appropriate to the micro-organism and the operation in question in order to ensure the protection of health of the general population and the environment.

2 Type B operations shall be considered in terms of their unit operations. The characteristics of each operation will dictate the physical containment to be used at that stage. This will allow the selection and design of process, plant and operating procedures best fitted to ensure adequate and safe containment. Two important factors to be considered when selecting the equipment needed to implement the containment are the risk of, and the effects consequent on, equipment failure. Engineering practice may require increasingly stringent standards to reduce the risks of failure as the consequence of that failure becomes less tolerable.

		Containment Levels		
	Specifications	*B2*	*B3*	*B4*
1	Viable micro-organisms should be contained in a system which physically separates the process from the environment (closed system)	Yes	Yes	Yes
2	Exhaust gases from the closed system should be treated so as to:	Minimise release	Prevent release	Prevent release
3	Sample collection, addition of materials to a closed system and transfer of viable micro-organisms to another closed system, should be performed so as to:	Minimise release	Prevent release	Prevent release
4	Bulk culture fluids should not be removed from the closed system unless the viable micro-organisms have been:	Inactivated by validated means	Inactivated by validated chemical or physical means	Inactivated by validated chemical or physical means
5	Seals should be designed so as to:	Minimise release	Prevent release	Prevent release
6	Closed systems should be located within a controlled area	Optional	Optional	Yes, and purpose-built

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Schedule

	Specifications	*Containment Levels*		
		B2	*B3*	*B4*
(a)	Biohazard signs should be posted	Optional	Yes	Yes
(b)	Access should be restricted to nominated personnel only	Optional	Yes	Yes, via airlock
(c)	Personnel should wear protective clothing	Yes, work clothing	Yes	Yes. A complete change
(d)	Decontamination and washing facilities should be provided for personnel	Yes	Yes	Yes
(e)	Personnel should shower before leaving the controlled area	No	Optional	Yes
(f)	Effluent from sinks and showers should be collected and inactivated before release	No	Optional	Yes
(g)	The controlled area should be adequately ventilated to minimise air contamination	Optional	Optional	Yes
(h)	The controlled areas should be maintained at an air pressure negative to atmosphere	No	Optional	Yes
(i)	Input air and extract air to the controlled area should be HEPA filtered	No	Optional	Yes
(j)	The controlled area should be designed to contain spillage of the entire contents of the closed system	Optional	Yes	Yes
(k)	The controlled area should be sealable to permit fumigation	No	Optional	Yes
7	Effluent treatment before final discharge	Inactivated by validated means	Inactivated by validated chemical or physical means	Inactivated by validated physical means

6

Appendix 1

Guidelines for the classification of genetically modified micro-organisms into Group I according to Article 4(3) of Directive 90/219/EEC

For classification of GMMs into Group I, the following guidelines should be used for the further interpretation of the criteria established by Annex II of Directive 90/219/EEC, and for the further development by Competent Authorities of more detailed guidelines aimed at specific cases.

1 Criteria (i) - (iii) refer to immunocompetent humans and healthy animals or plants.

2 As regards criterion (i) of Annex II, the following guidelines are given:

(a) in deciding whether the recipient or parental micro-organism is likely to cause disease to animals or plants, consideration should be given to the environment likely to be exposed to the recipient or parental micro-organism;

(b) non-virulent strains of acknowledged pathogenic species could be considered as unlikely to cause disease and as satisfying criterion (i) in Annex II, provided that:

(i) the non-virulent strain has an established record of safety in the laboratory and/or industry with no adverse effects on human, animal or plant health;

and/or

(ii) the strain is stably deficient in genetic material that determines virulence, or has stable mutations known to sufficiently reduce virulence. When it is not essential to remove all virulence determinants from a pathogen, particular attention should be paid to any toxin genes, plasmid, or phageborne virulence determinants and harmful adventitious agents. On such occasions a case-by-case evaluation will be needed.

3 As regards criterion (ii) of Annex II, the following guidelines are given:

(a) The vector/insert should not contain genes expressing an active protein or transcript (eg virulence determinants, toxins, etc) at a level and in a form which endow the genetically modified micro-organism with a phenotype likely to cause disease to humans, animals or plants.

In any case, when the vector/insert contains sequences which are involved in the expression of harmful traits in certain micro-organisms, but which do not endow the GMM with a phenotype likely to cause disease to humans, animals or plants, or likely to cause adverse effects on the environment, then the vector/insert should not be self-transmissible and should be poorly mobilisable.

(b) In the case of Type B operations, special consideration should be given to the following:

(i) vectors should not be self-transmissible or contain functional transposing sequences, and should be poorly mobilisable;

(ii) in deciding whether the vectors/inserts are likely to endow the

genetically modified micro-organism with a phenotype likely to cause disease to humans, animals or plants or to cause adverse effects in the environment, it is important to ensure that the vectors/inserts are well characterised or limited in size as much as possible to the genetic sequences required to perform the intended function.

4 As regards criterion (iii) of Annex II, the following guidelines are given:

(a) In deciding whether the genetically modified micro-organism is likely to cause adverse effects on the environment or disease to animals or plants, consideration should be given to the environment likely to be exposed to the GMMs.

(b) In the case of Type B operations, in addition to criterion (iii), special consideration should be given to the following:

(i) the genetically modified micro-organism should not transfer any resistance markers to micro-organisms, if such transfer could compromise disease treatment;

(ii) the genetically modified micro-organism should be as safe in the industrial setting as the recipient or parental micro-organism, or have characteristics that limit survival and gene transfer.

(c) Other GMMs which could be included in Group I if they are without adverse effects on the environment and meet the conditions in Annex II (i) are those that are constructed entirely from a single prokaryotic recipient (including its indigenous plasmids, transposons and viruses), or from a single eukaryotic recipient (including its chloroplasts, mitochondria, plasmids, but excluding viruses), **or** consist entirely of genetic sequences from different species that exchange these sequences by known physiological processes.

Before deciding if these GMMs are to be included in Group I, it should be considered whether they are excluded from the Directive under the provisions of Annex I B (4) and taking into account that self-cloning means the removal of nucleic acid from a cell of an organism, followed by reinsertion of all or part of that nucleic acid - with or without further enzymic chemical or mechanical steps - into the same cell type (or cell-line) or into cells of phylogenetically closely related species which can naturally exchange genetic material with the donor species.

Appendix 2

Current subjects covered in HSE/ACGM guidance

Application of health and safety legislation to GMOs

- *Genetic modification and COSHH*
- *Oncogenes and COSHH*
- *Management of Health and Safety at Work Regulations 1992*
- *Genetic modification safety committees*
- *Health surveillance*

Risk assessment of GMOs

- *Risk assessment of GMMs other than viruses*
- *Risk assessment of human and animal viruses*
- *Risk assessment of plant viruses*
- *Risk assessment of GM plants*
- *Risk assessment of transgenic animals*

Containment and control measures

- *Laboratory and large-scale measures for micro-organisms*
- *Glasshouse and growth-rooms*
- *Animal facilities*

Miscellaneous

- Risk assessment examples

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Stanley Precinct
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Appendix 3

Format for information to be supplied with accident notification* (regulation 14)

1 *General data*

Date and time of the accident:
Name and address of person responsible for carrying out the activity:

.....

.....

Address of premises where activity is carried out:

.....

.....

Grid reference:
Principal activity of installation .....

.....

Type of activity (Type A or Type B):
Classification of organism (Group I or Group II)

2 *Type of accident*

Failure of equipment (breakage/leakage etc)
Fire
Explosion
Maloperation of equipment (human/mechanical)
Other (specify) .....

3 *Organisms released*

Identity of genetically modified organisms released:
Quantity of genetically modified organisms released:
Form and/or concentration in which organisms released:

4 *Description of the circumstances of the accident*

5 *Was there any emergency plan drawn up in advance?*

yes ☐ no ☐

If yes by whom?.....

6 *Emergency measures taken*

(a) Inside the installation .....
.....

(b) Outside the installation .....
.....

7 *Assumed or established cause(s) of accident* (If not known, information should be supplied as soon as possible)

*As agreed by the Committee of National Competent Authorities

8 *Nature and extent of exposure*

(a) Within the installation: provide information on the following:
- persons exposed to the accident
- casualties
- damage to health
- material damage
- damage affecting the containment equipment
- whether the danger is still present
- if danger still exists it should be specified

(b) Outside the installation/to the environment: provide information on the following:
- persons exposed to the accident
- casualties
- damage to health
- types of environments exposed (water, sewage systems, agricultural land, natural environments)
- material damage
- damage affecting the containment equipment
- damage to the environment
- whether the danger is still present
- if danger still exists it should be specified

9 *Member States already informed bilaterally of the accident*

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